

Fig 4

A

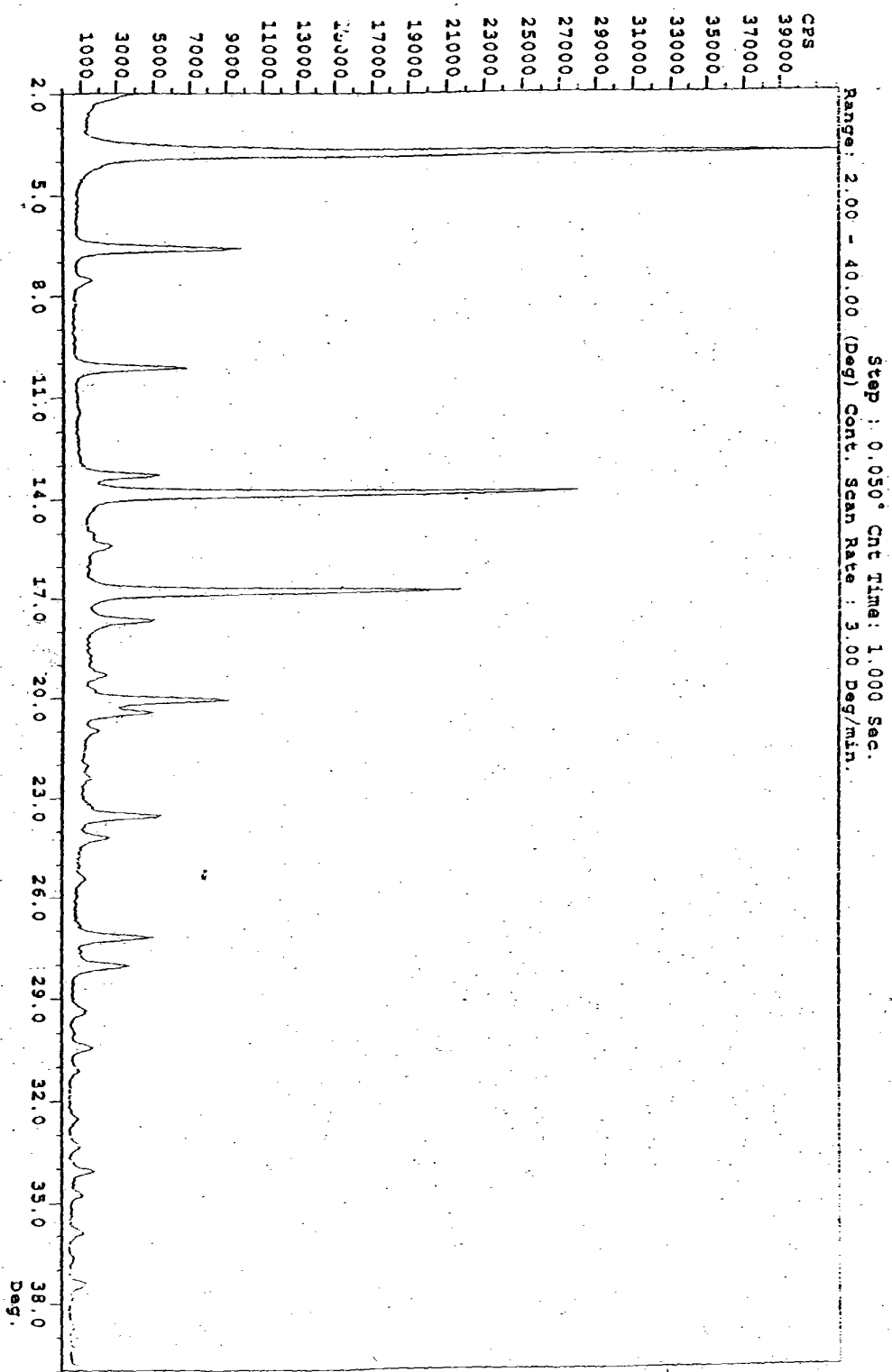


Fig. 2
C

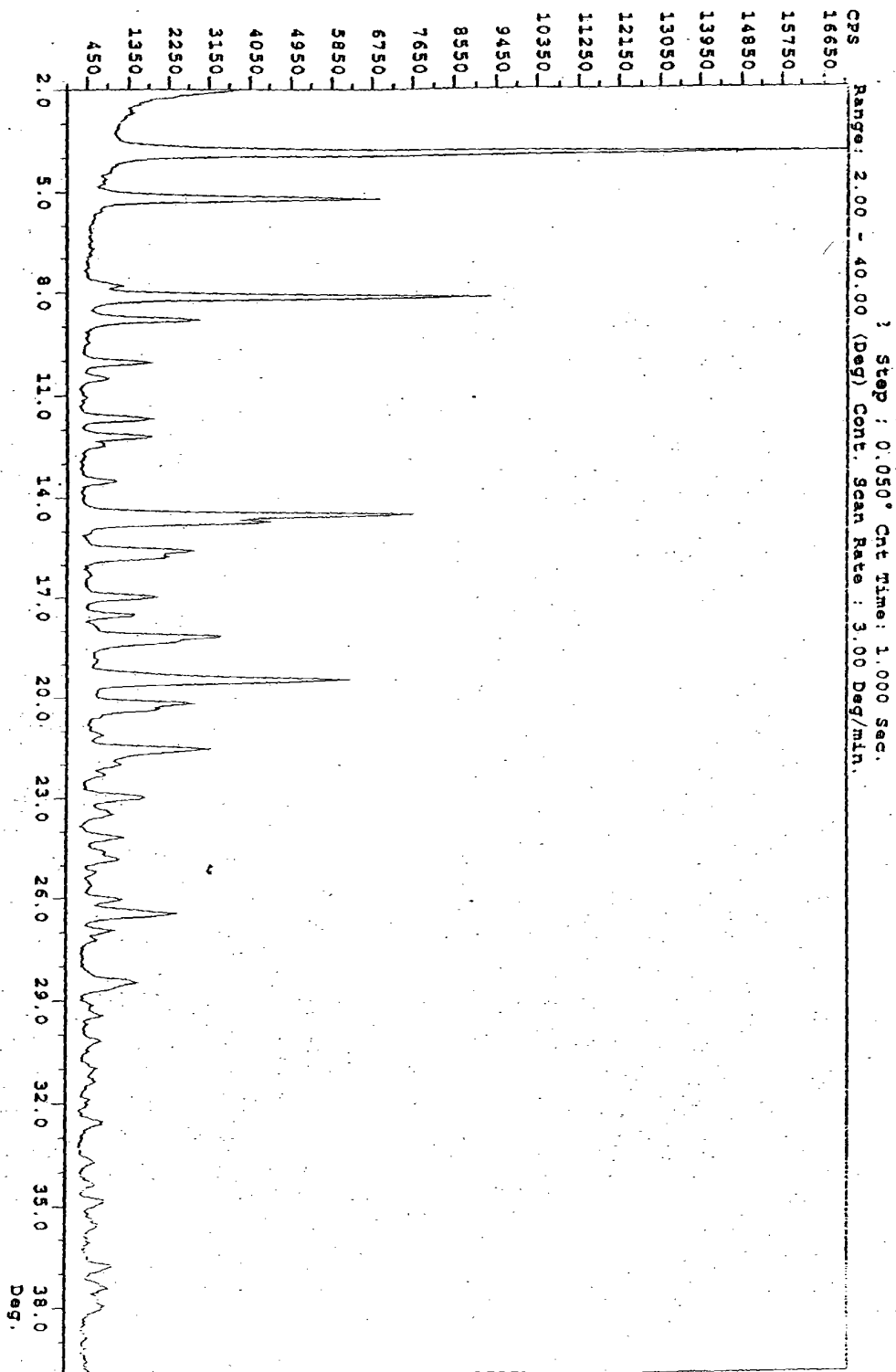


Fig 3 D

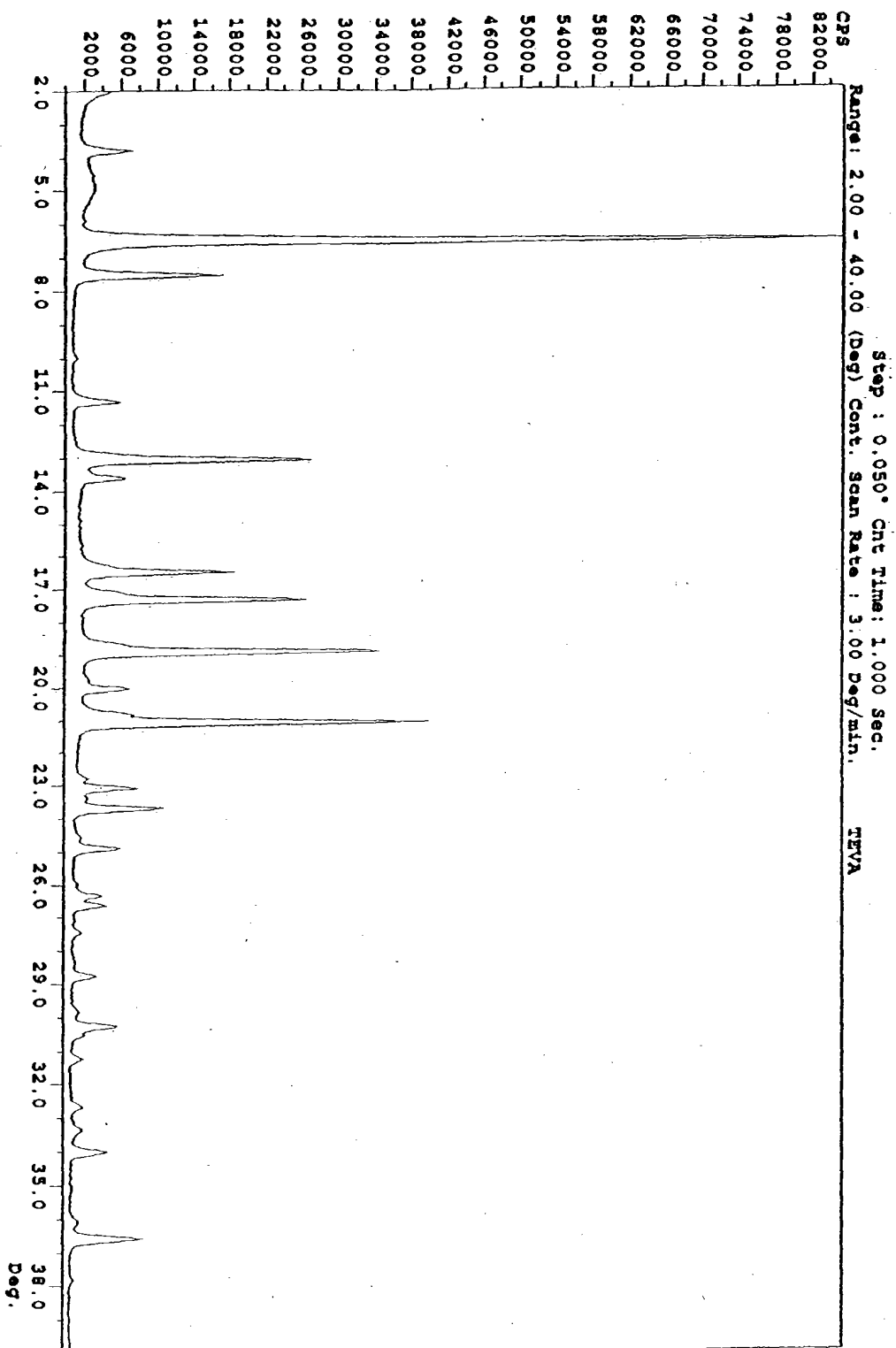


Fig 4 E

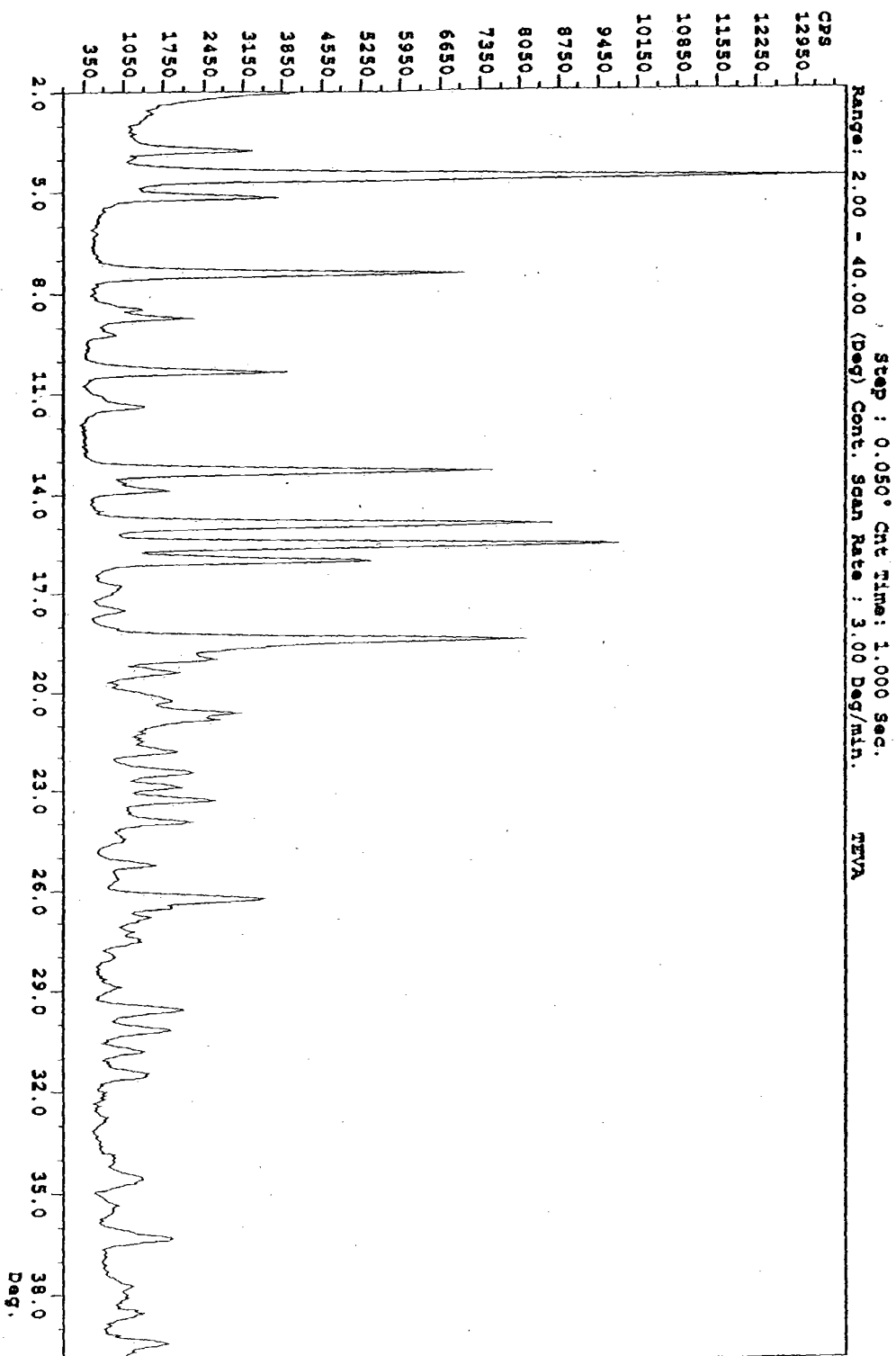


Fig. 5

=

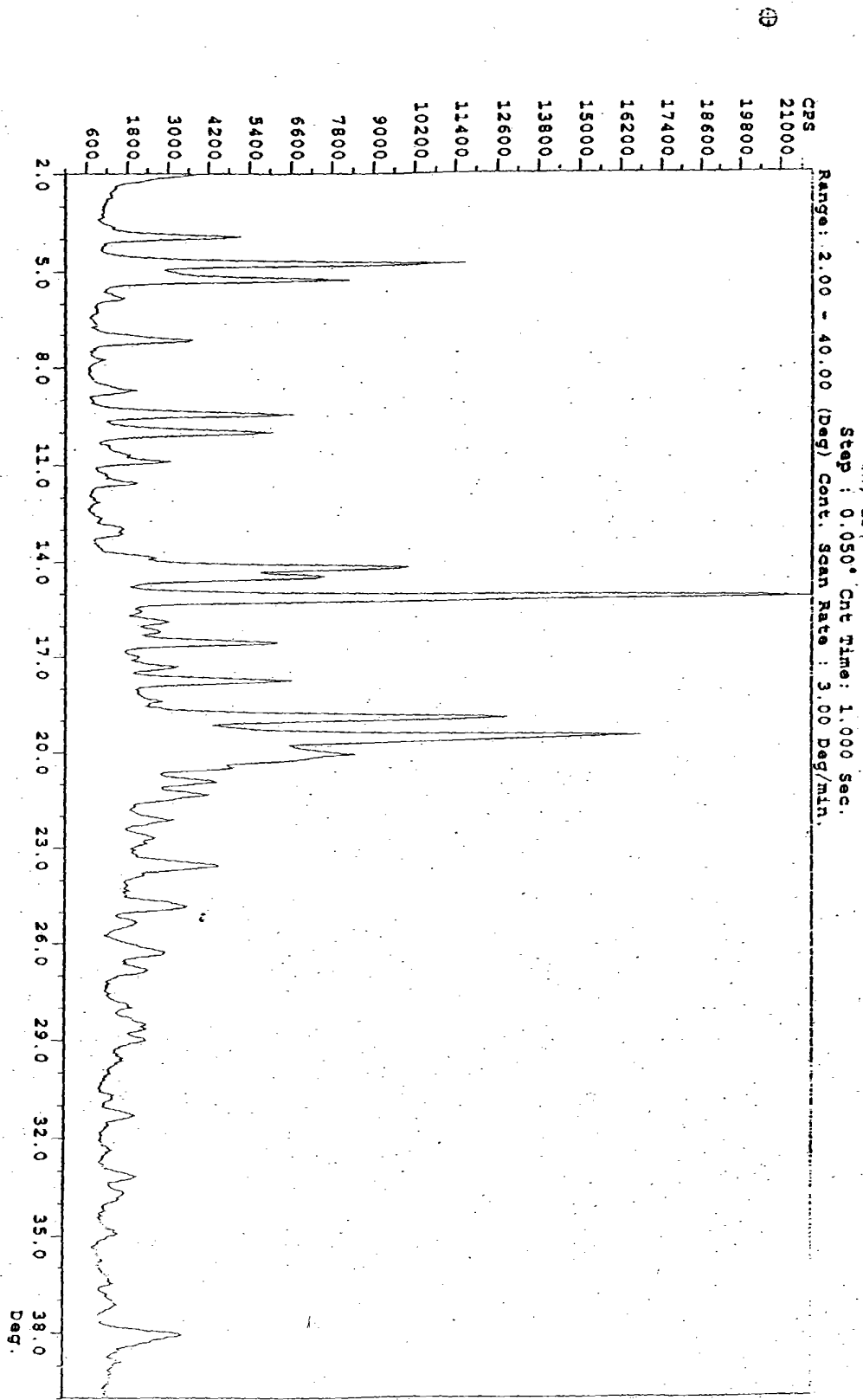


Fig. 6

G

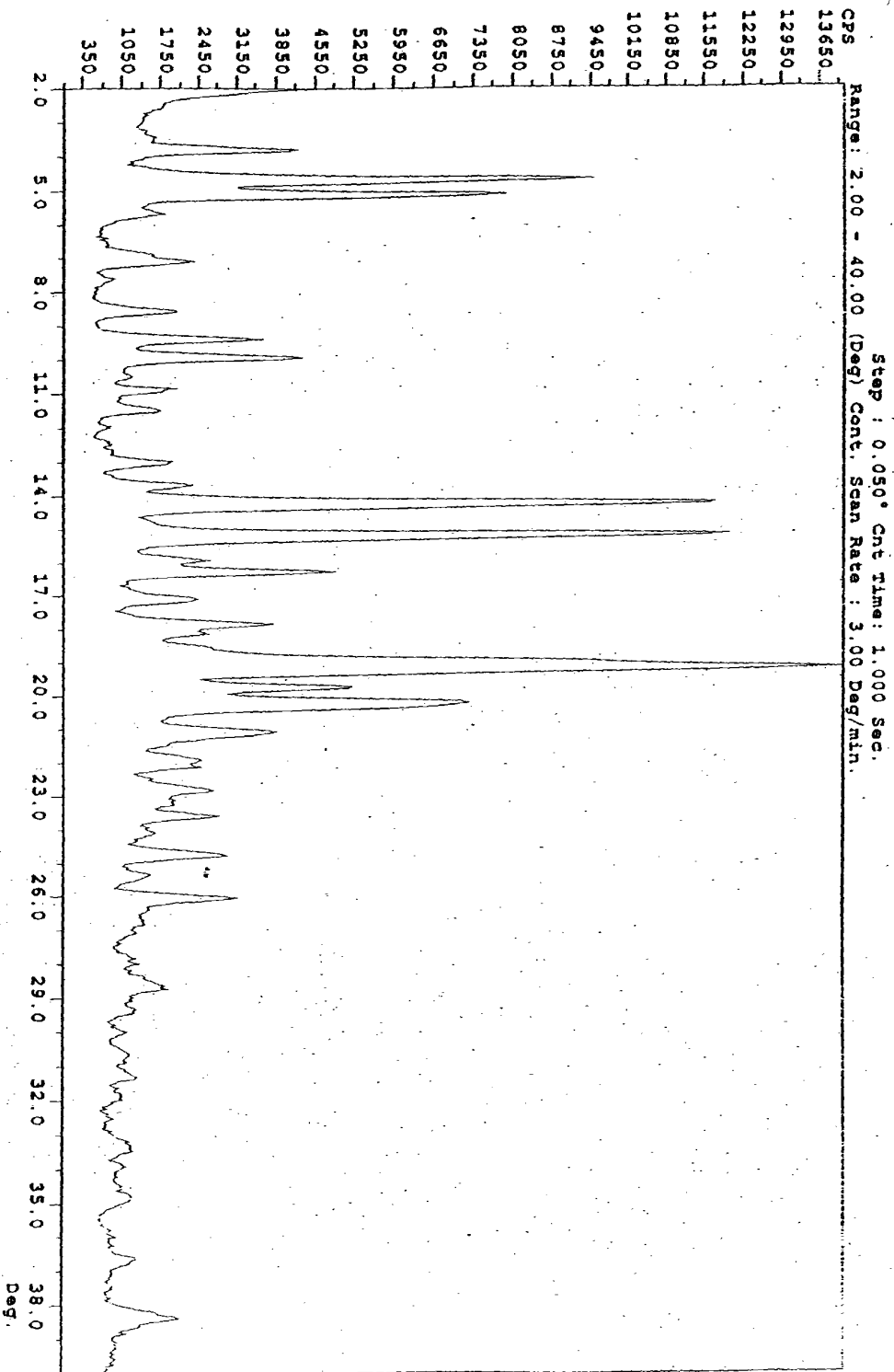


Fig 7

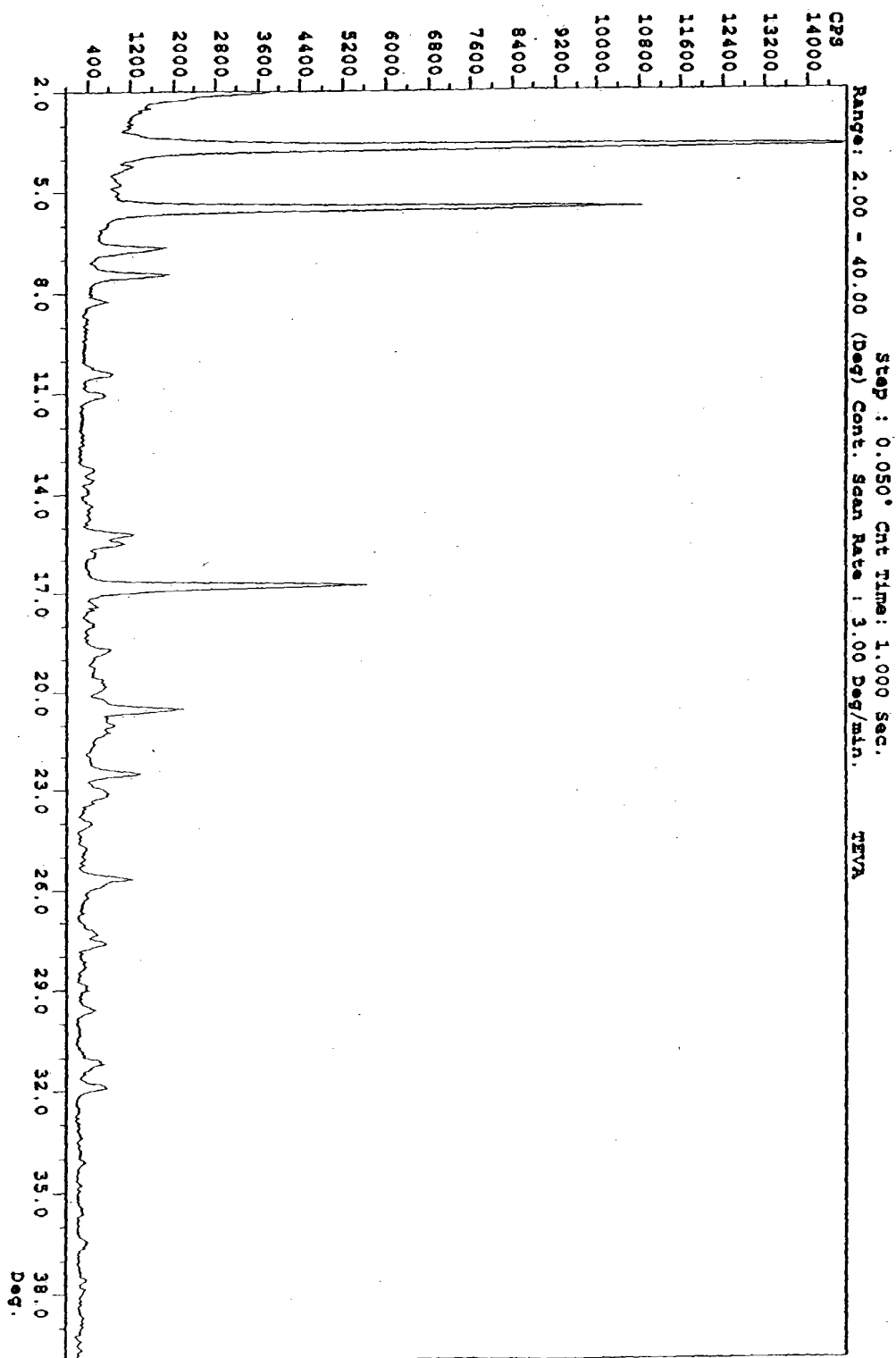


Fig. 8
5

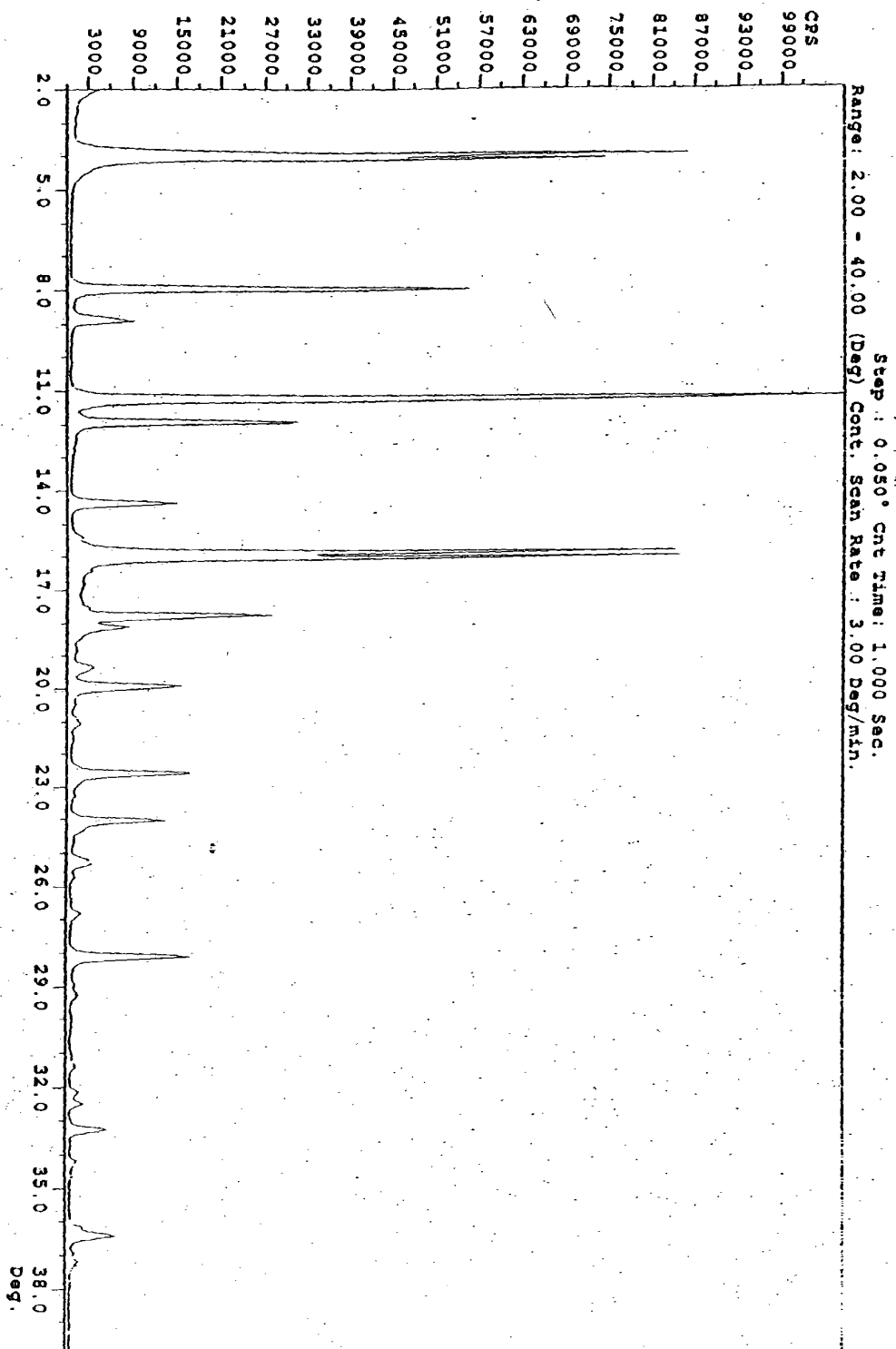


Fig. 9

1<

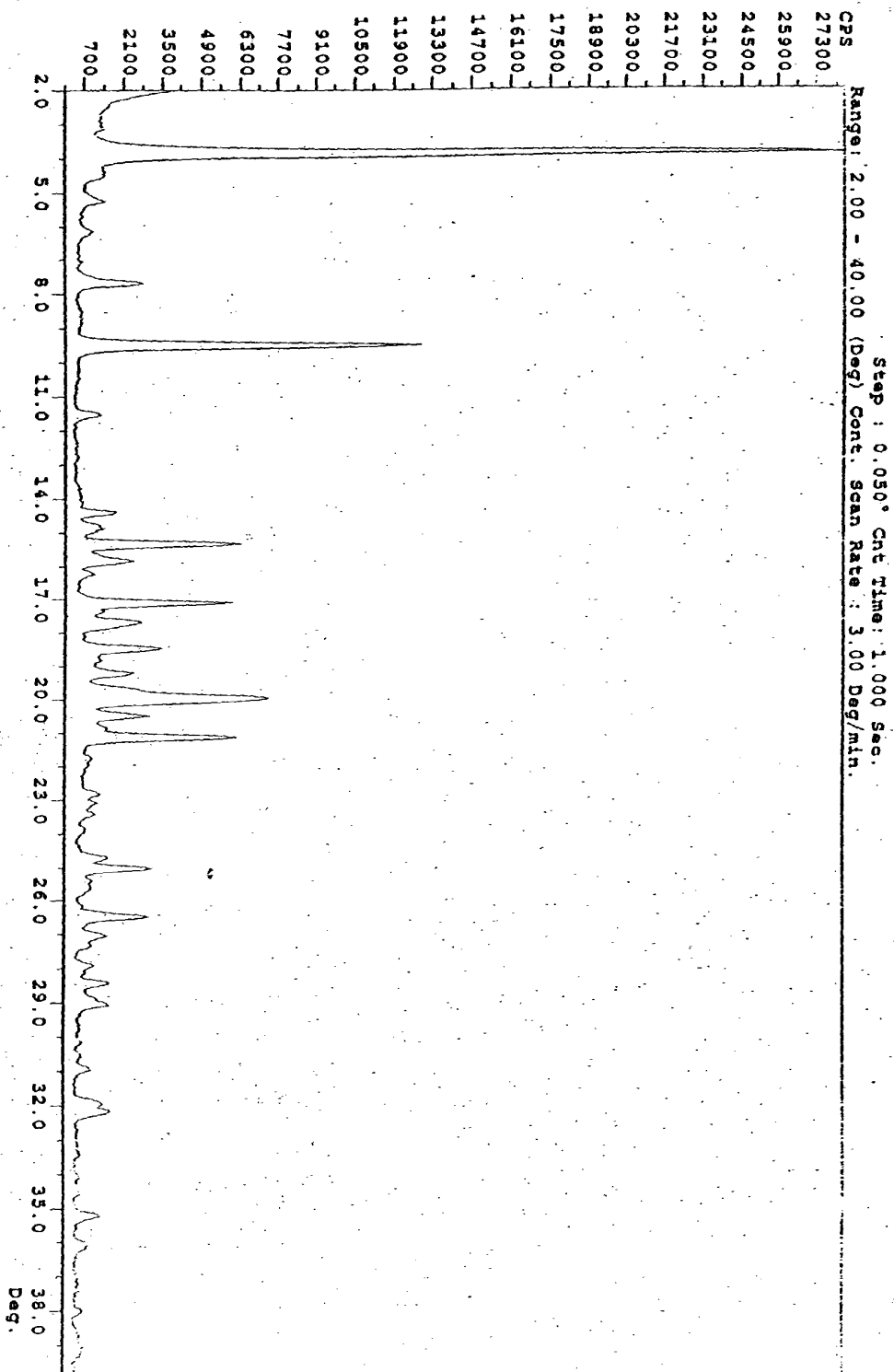


Fig. 10 L

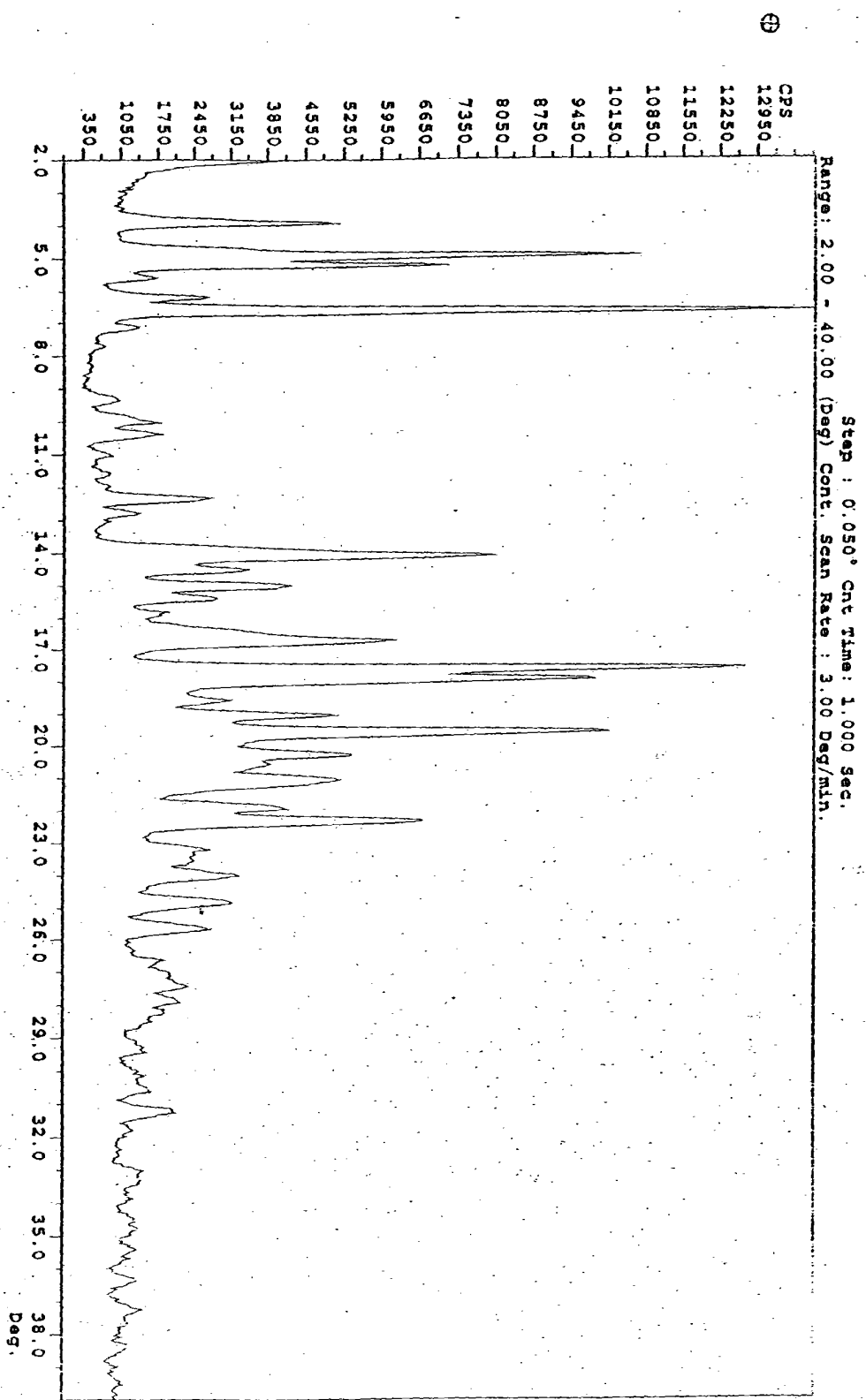
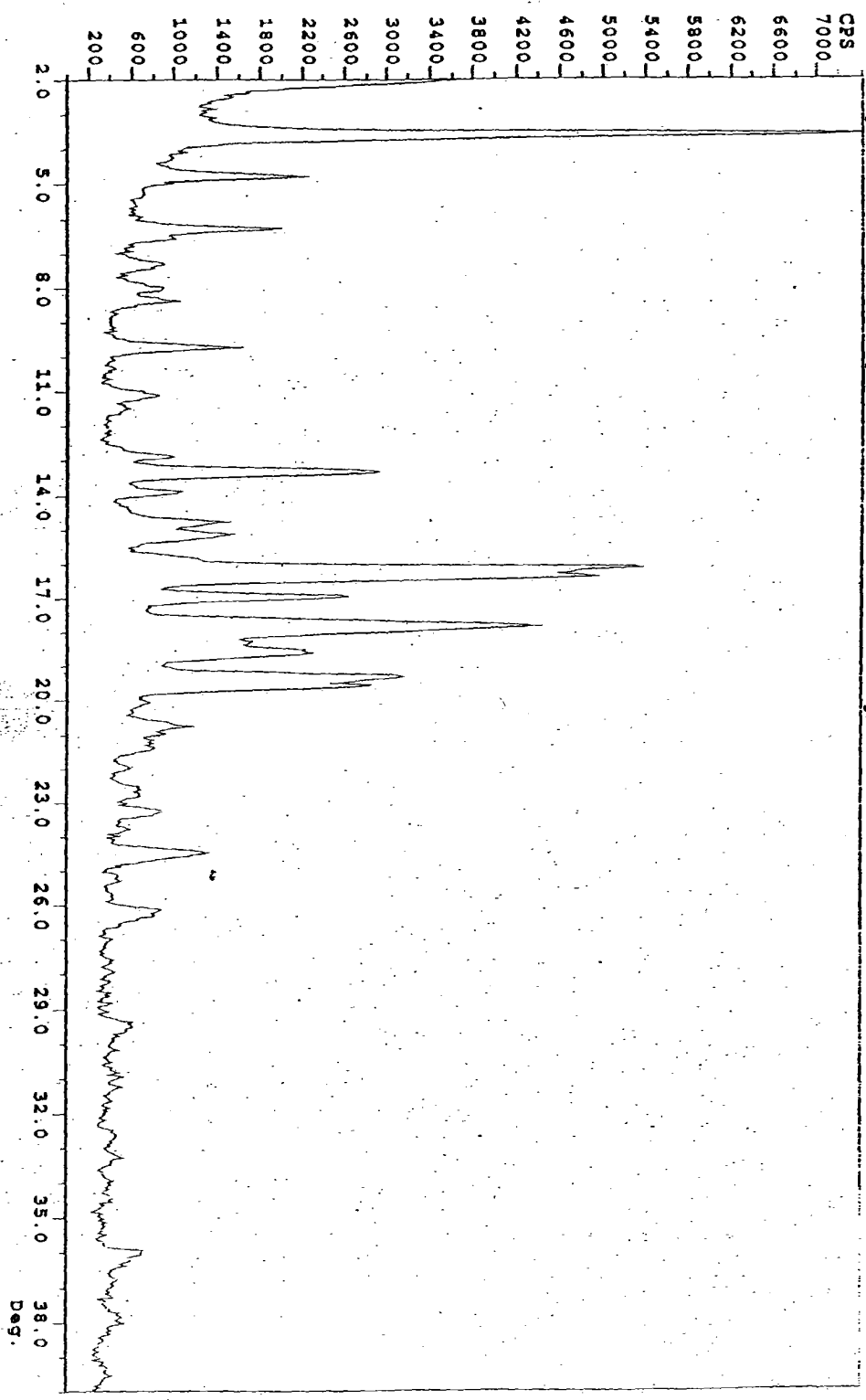


Fig. 11

M

Range: 2.00 - 40.00 (Deg) Step: 0.050° Cnt Time: 1.000 Sec.
Cont. Scan Rate: 3.00 Deg/min.



⊕

Fig. 12

N

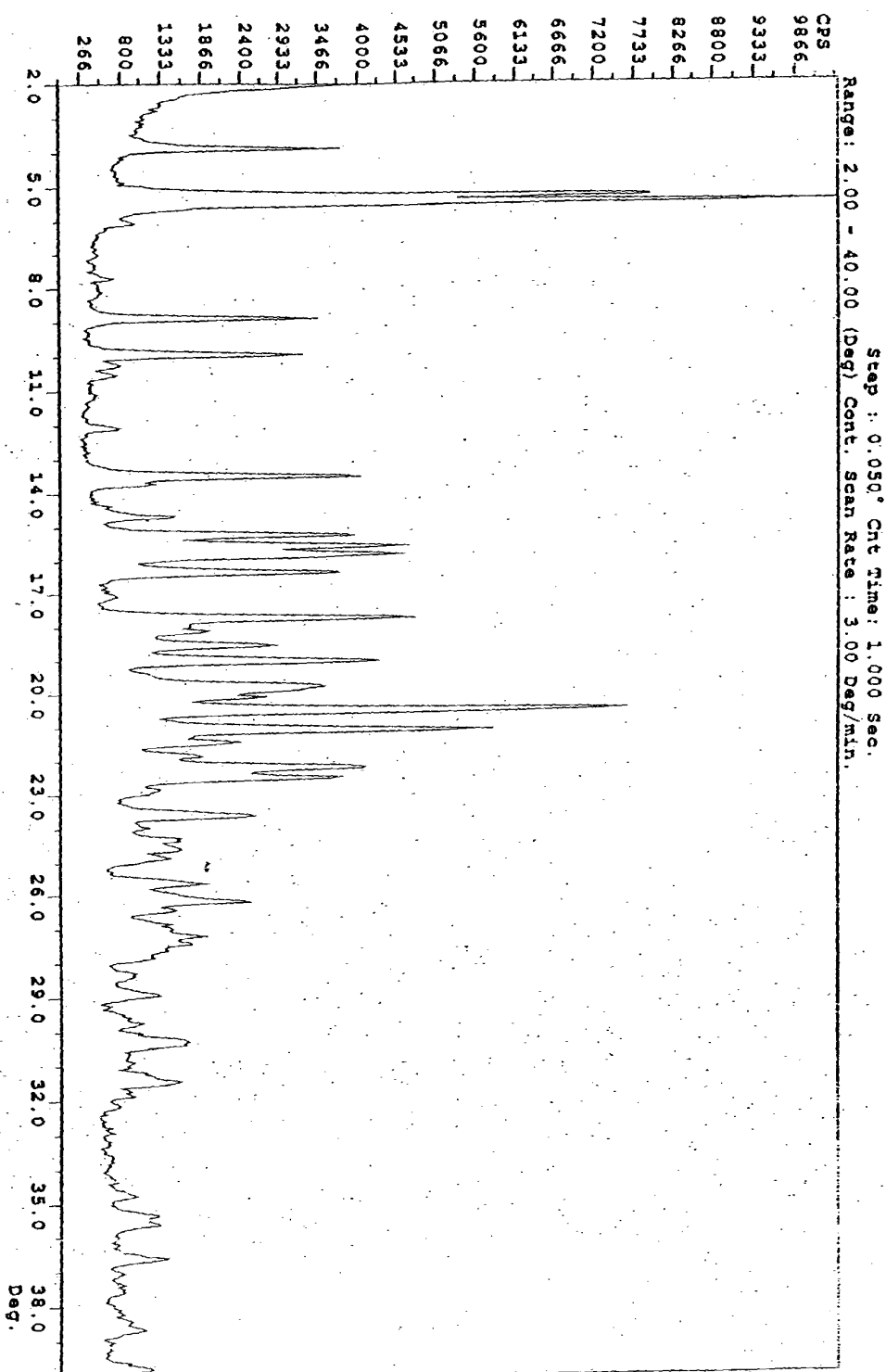


Fig. 13 0

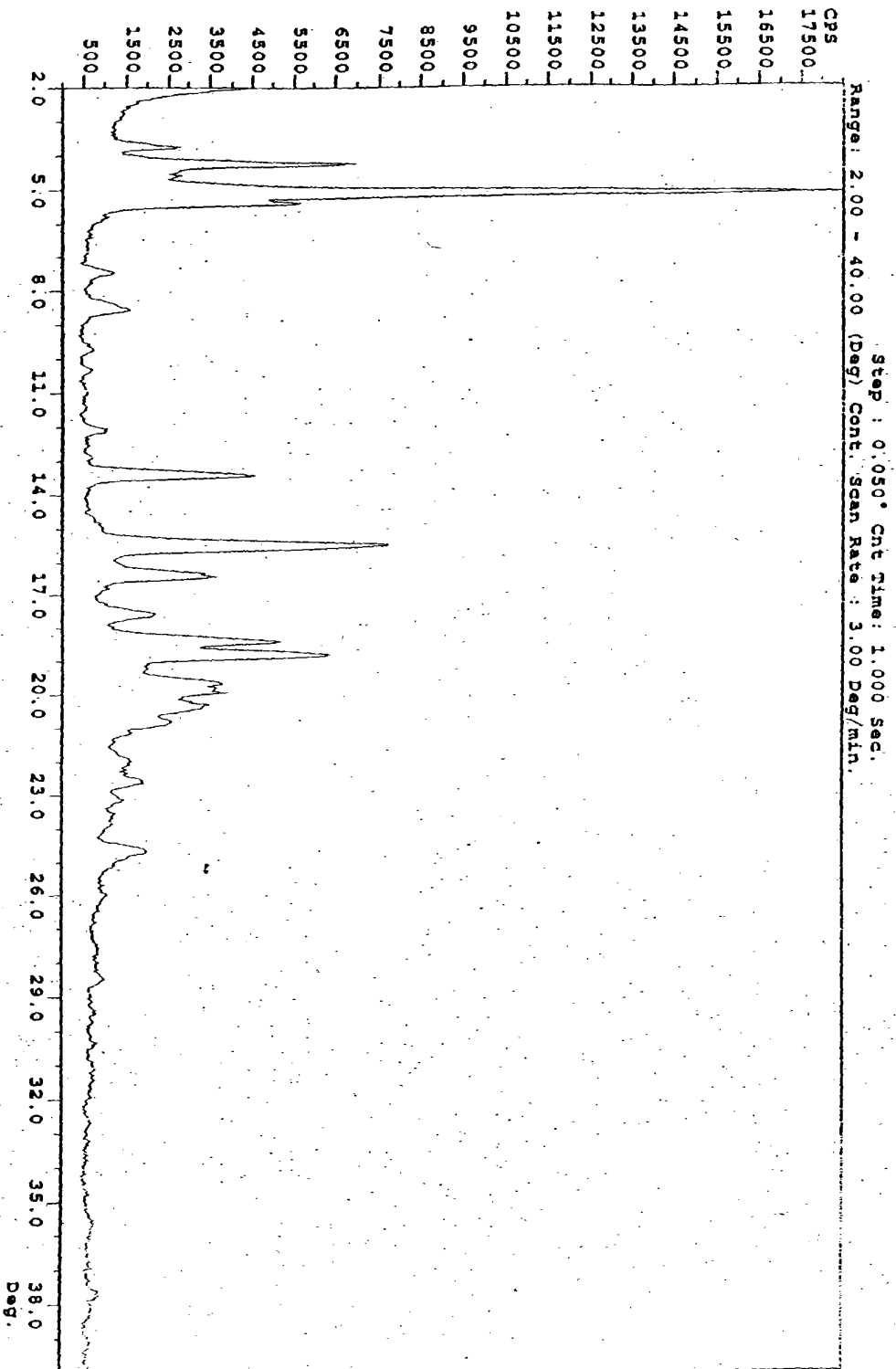


Fig. 14

P

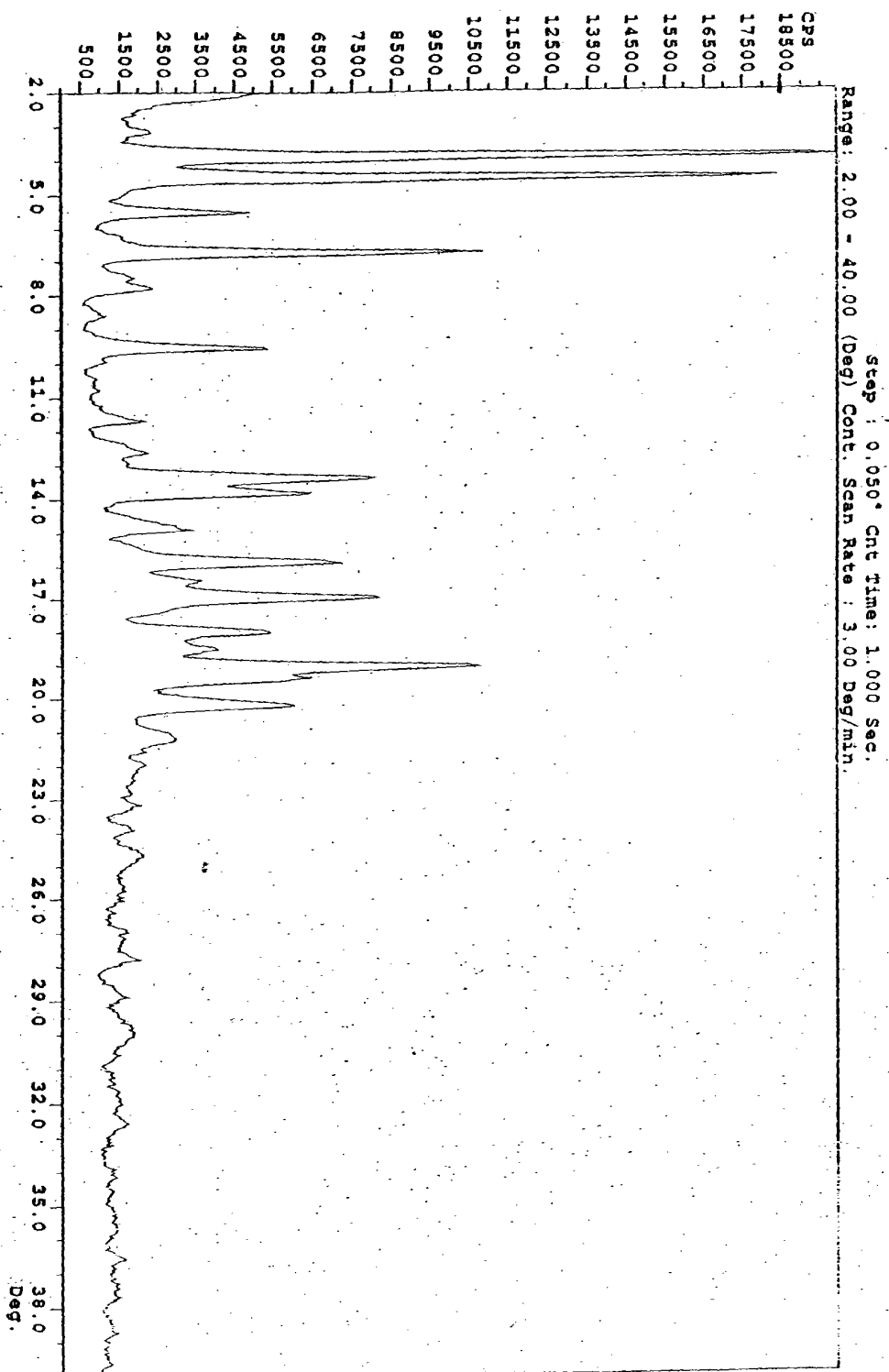


Fig. 15 Q

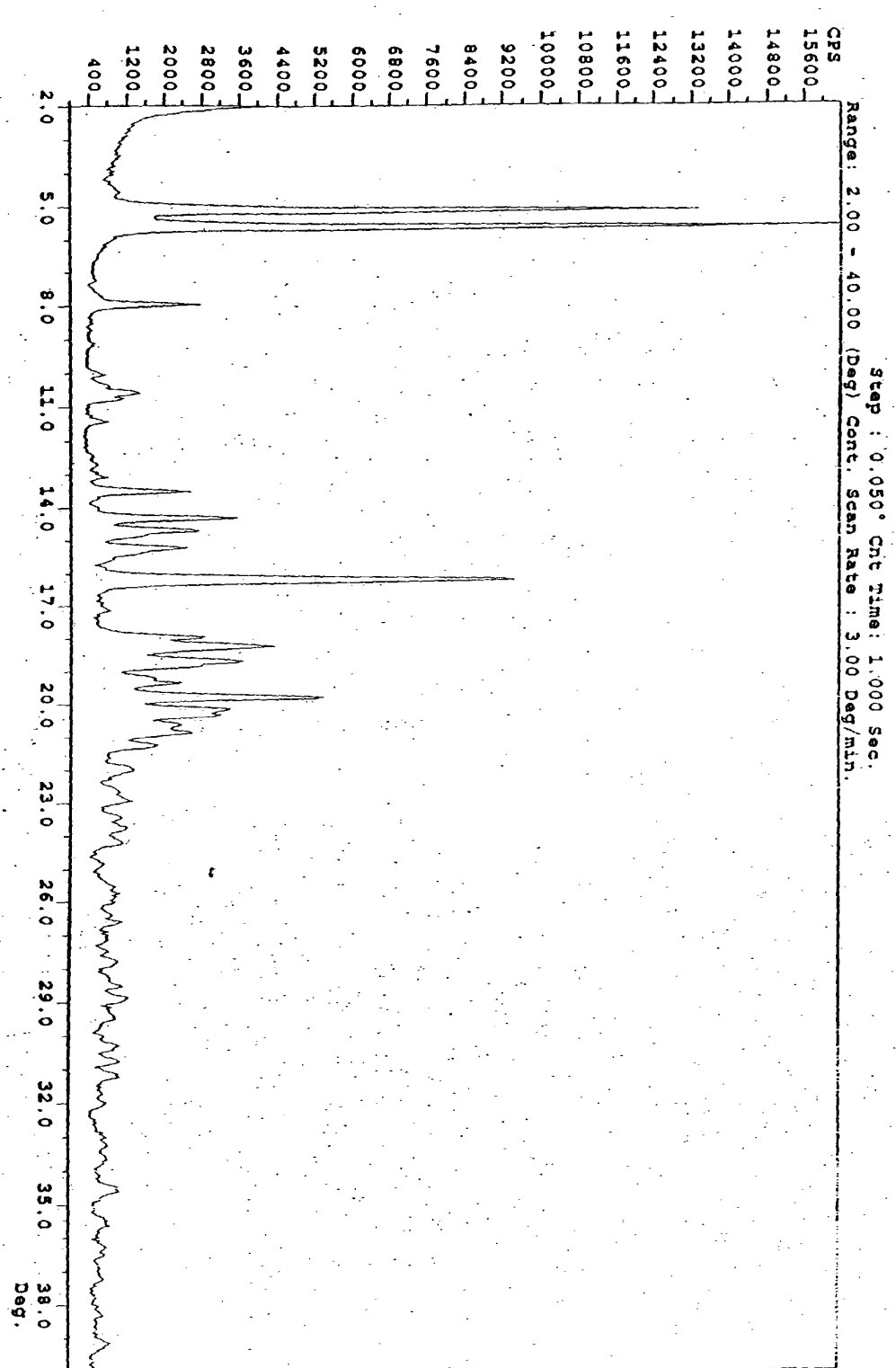


Fig. 16

T

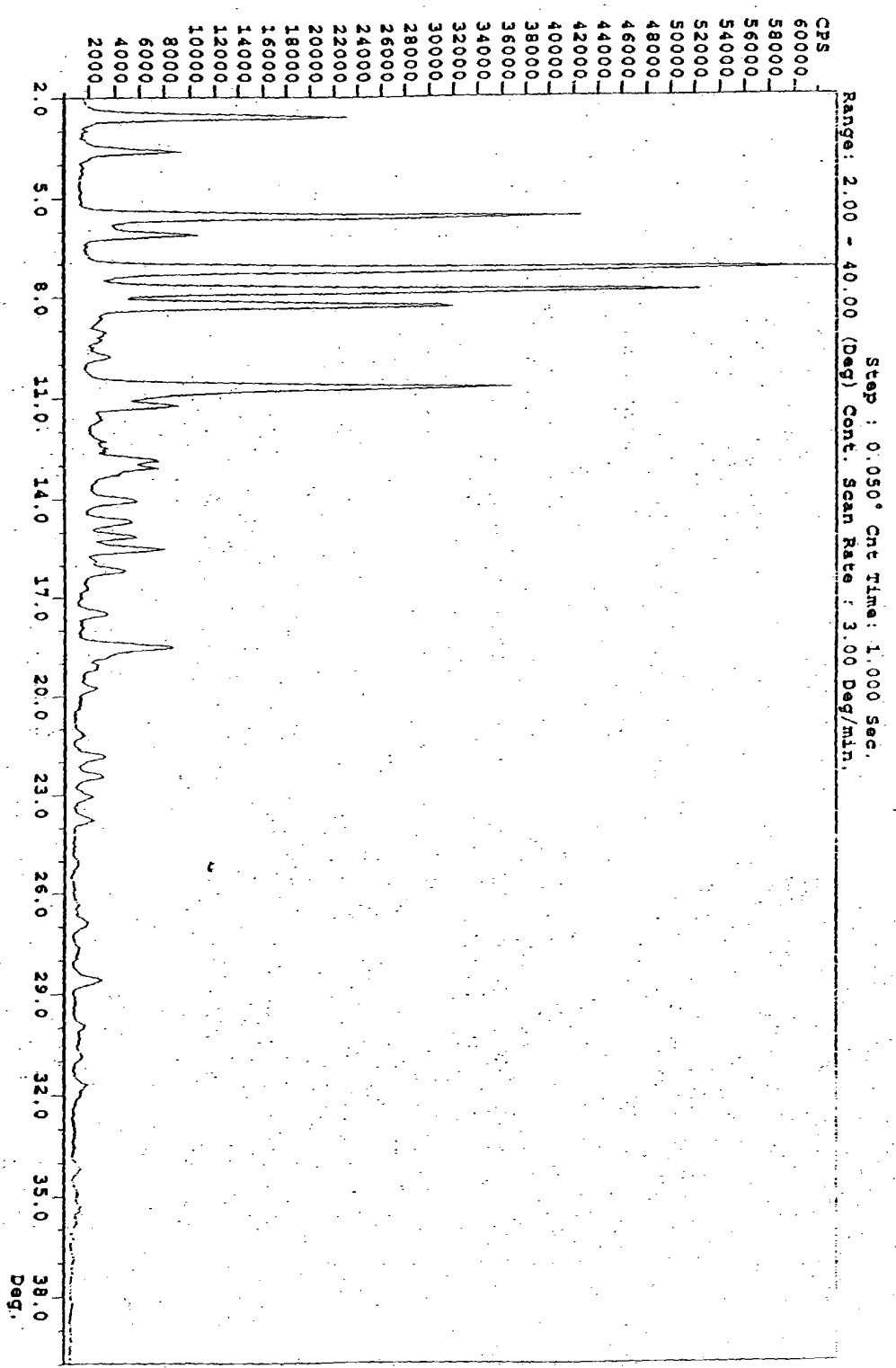
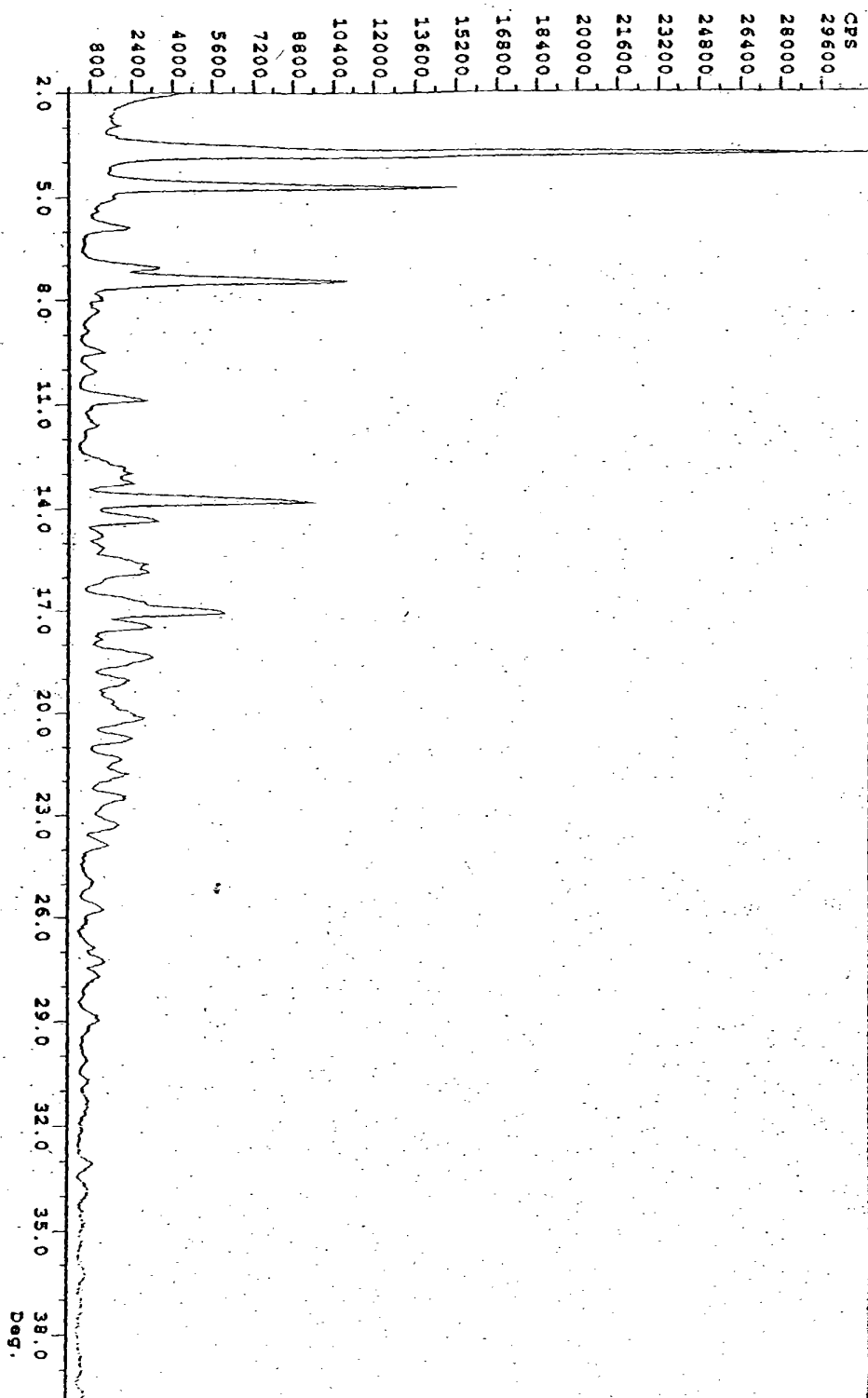


Fig. 17

u

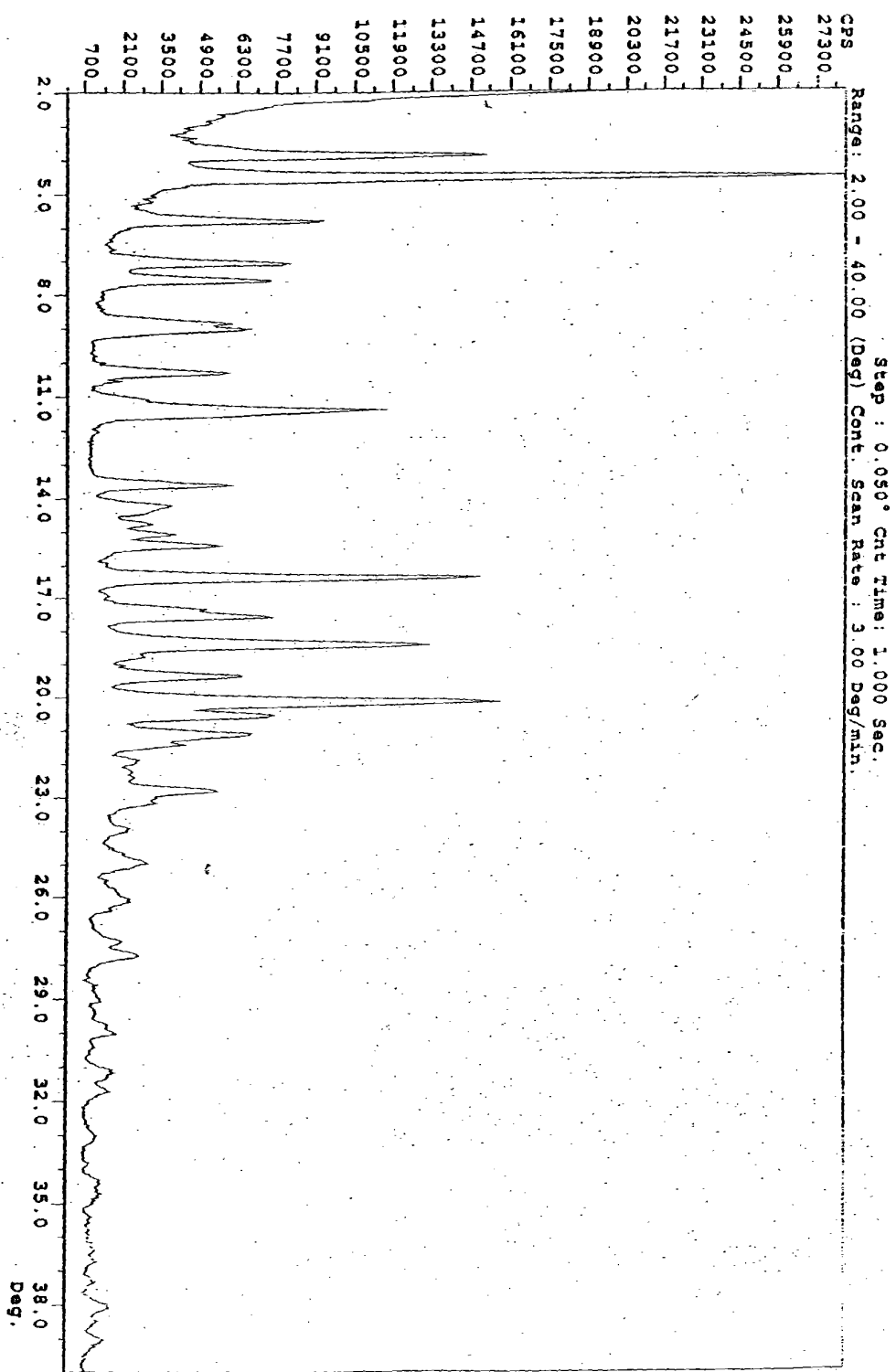
Step : 0.050° Cnt Time: 1.000 Sec.
Range: 2.00 - 40.00 (Deg) Cont. Scan Rate : 3.00 Deg/min.



⊕

Fig. 18

✓



⊕

fig 19

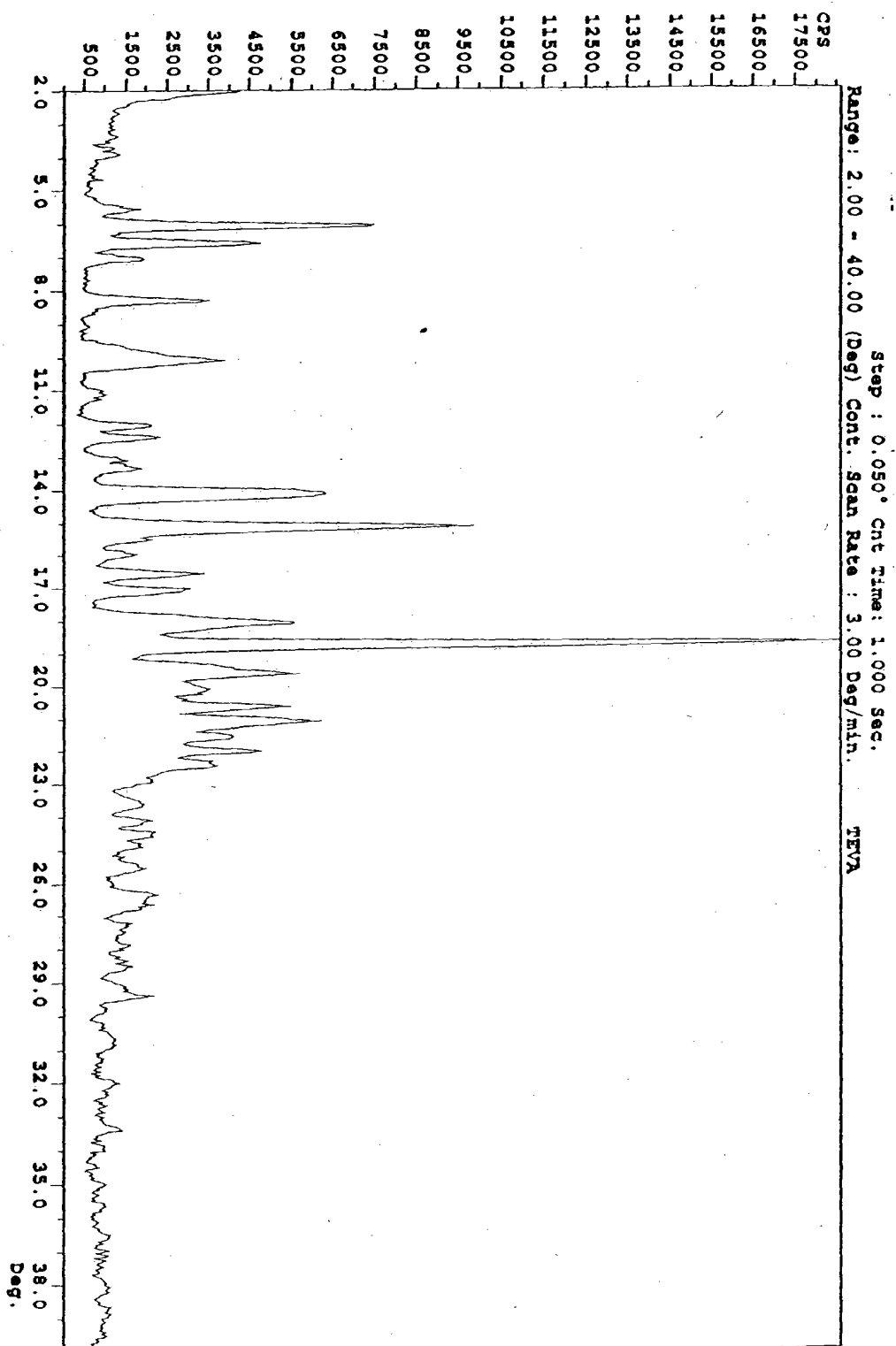


Figure 20 - Nateglinide Form Z

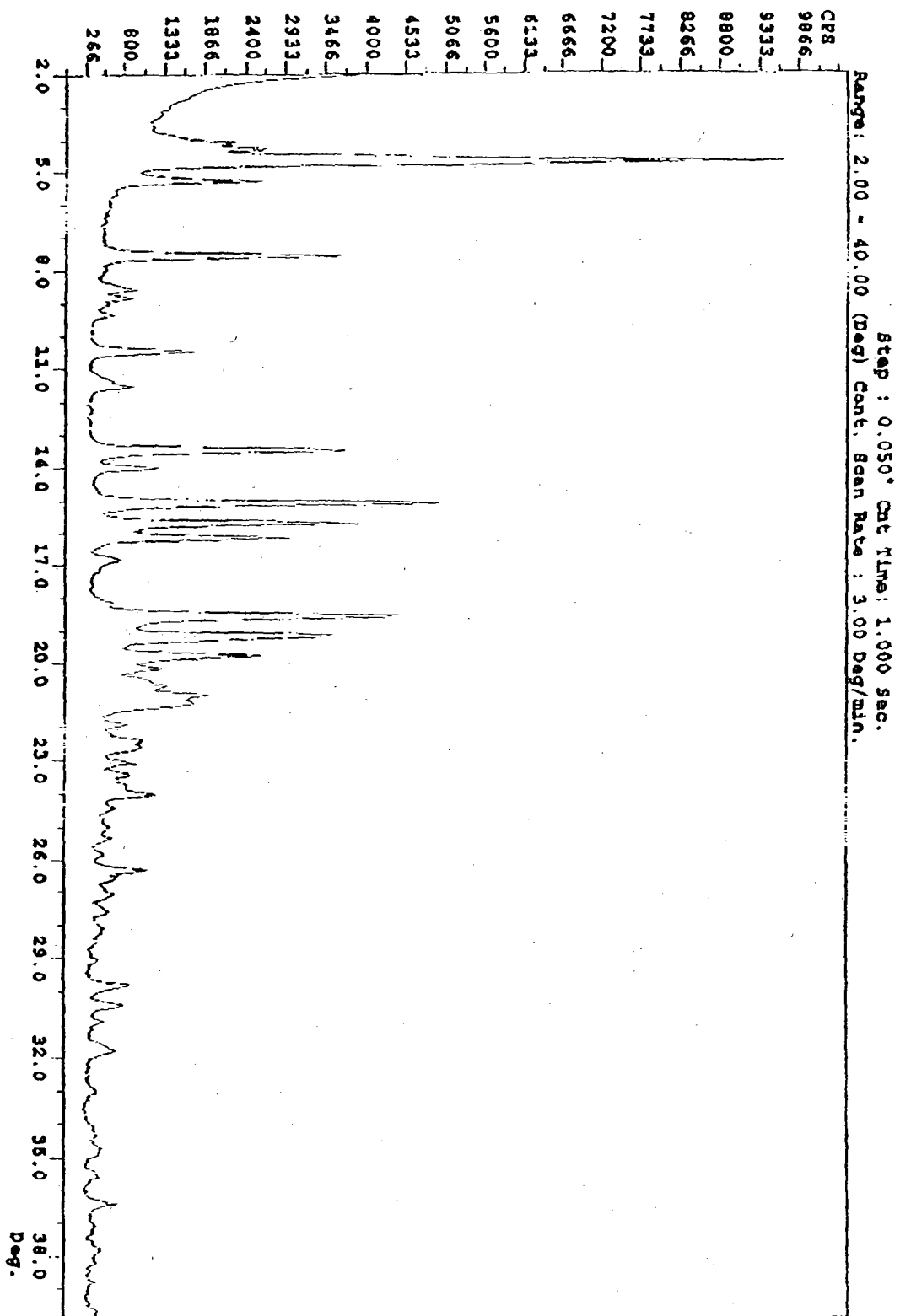


fig 2p 2

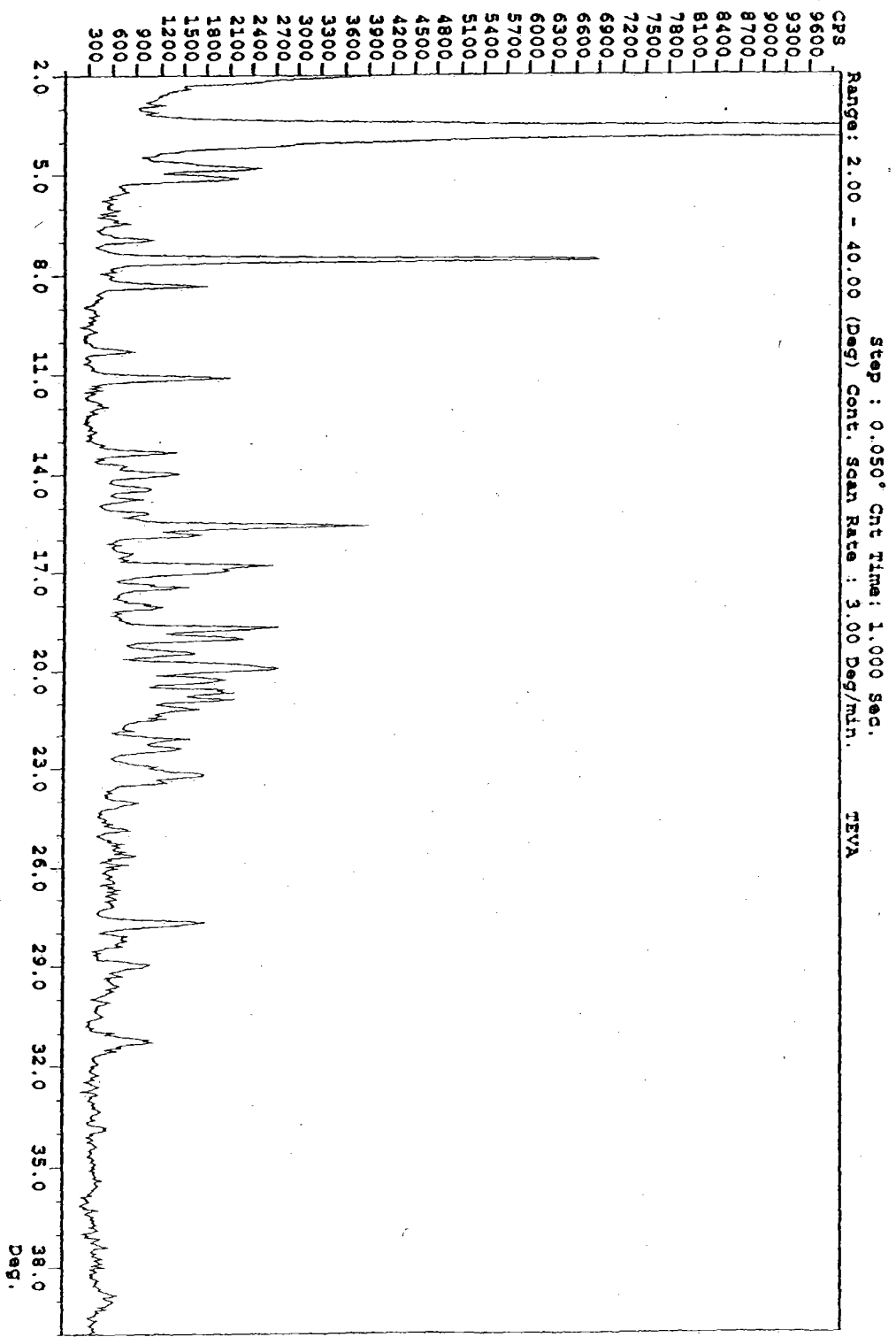


Fig. 22 B

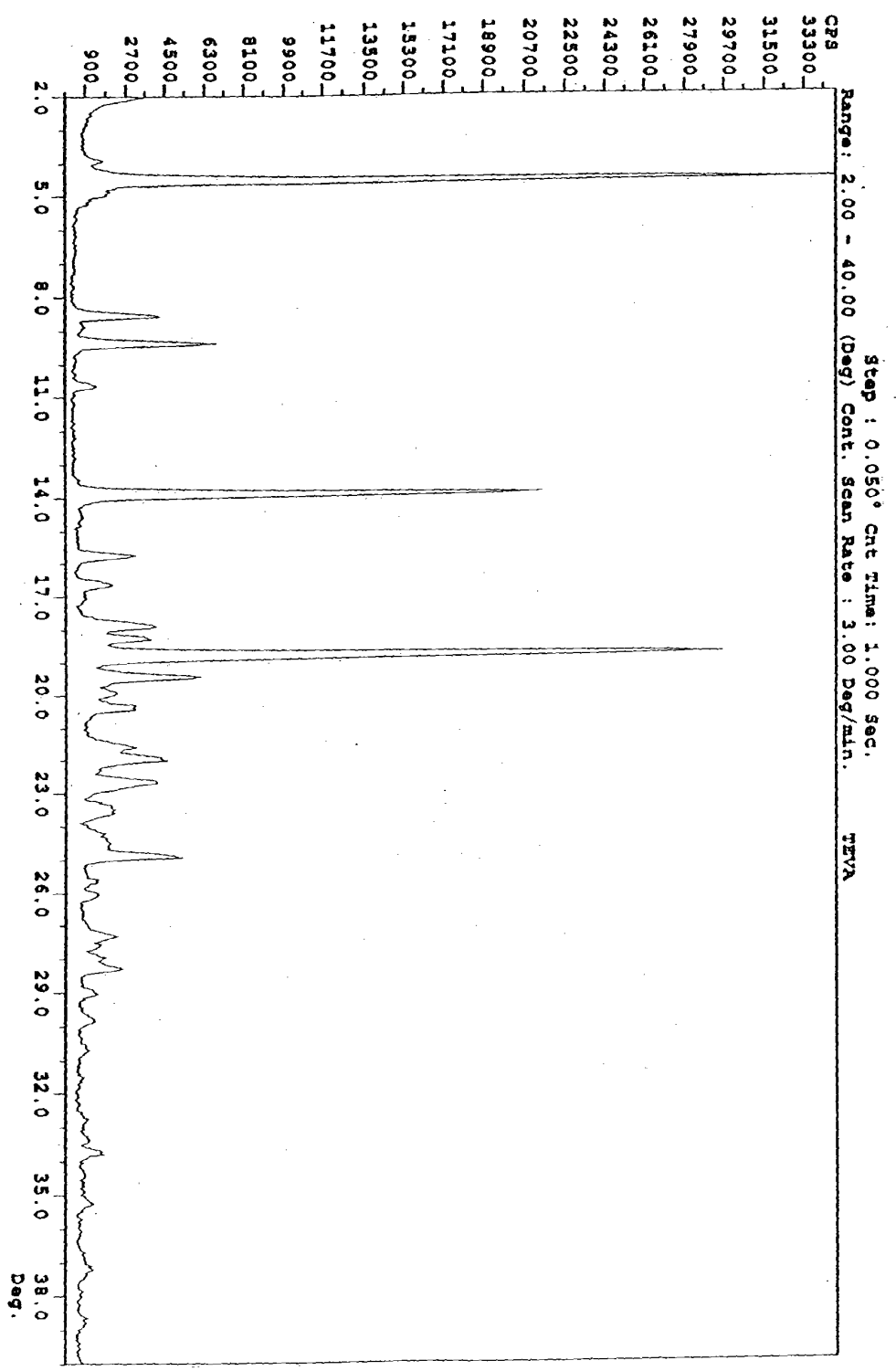


Fig 23 10

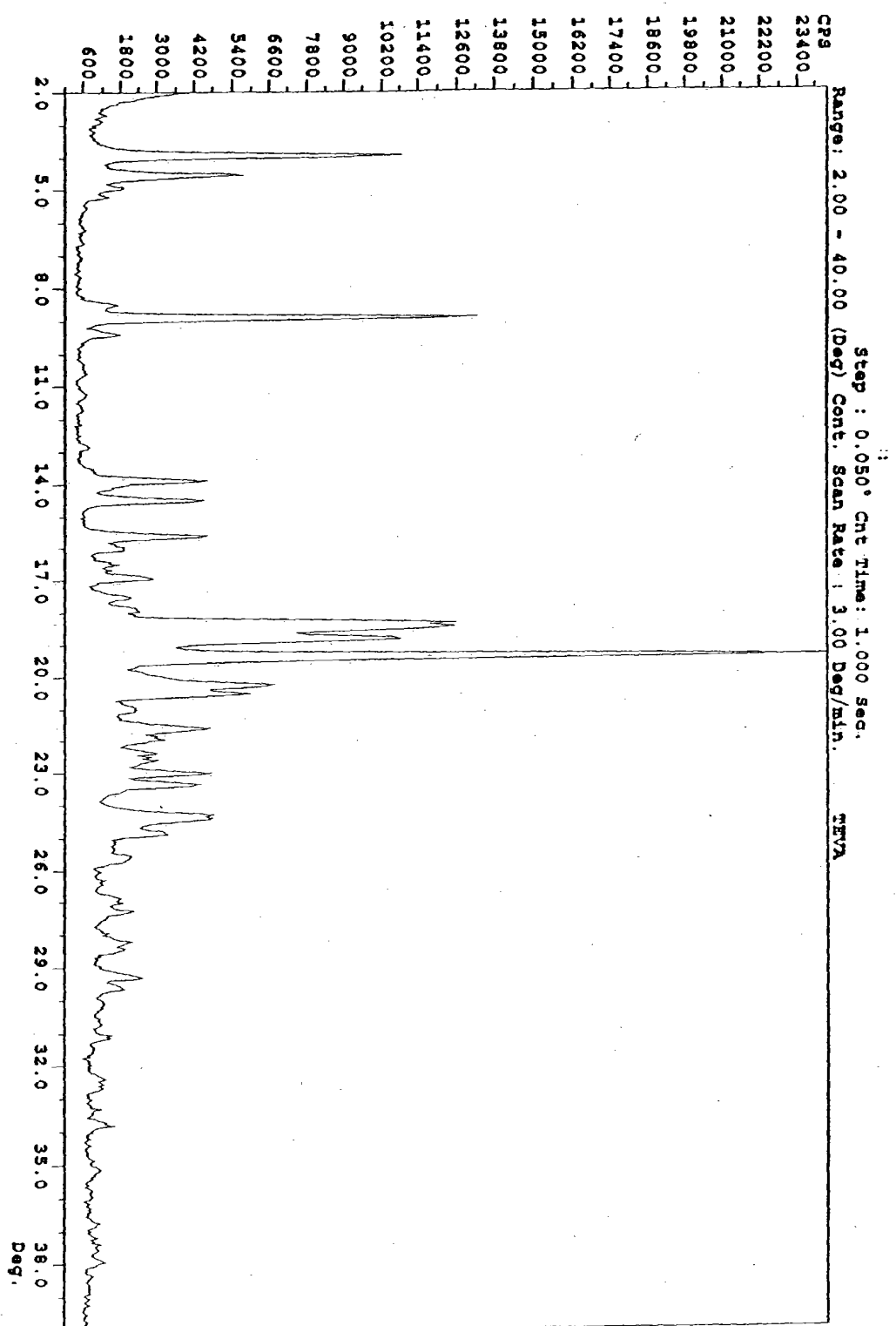


Fig 24 d

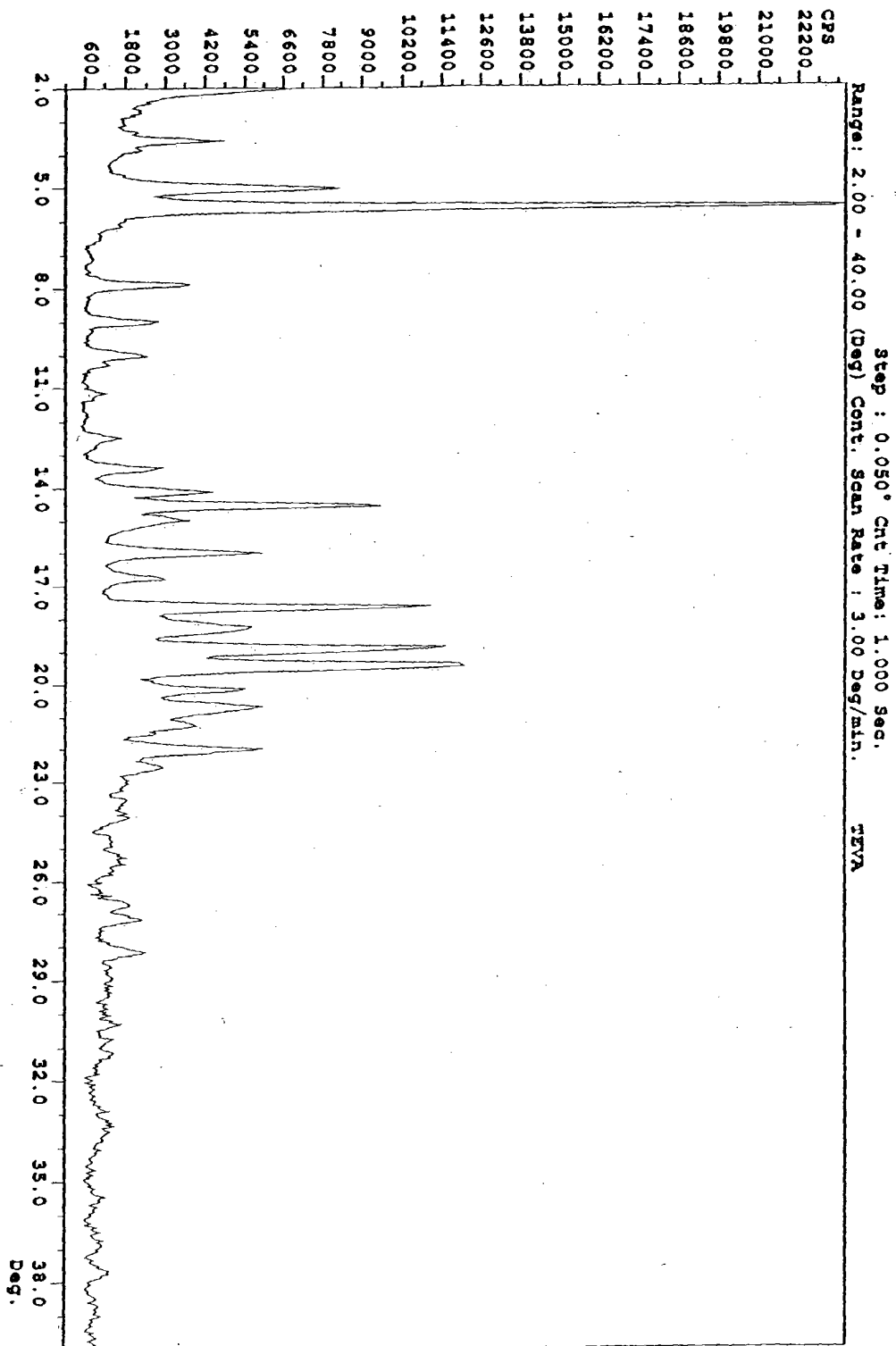
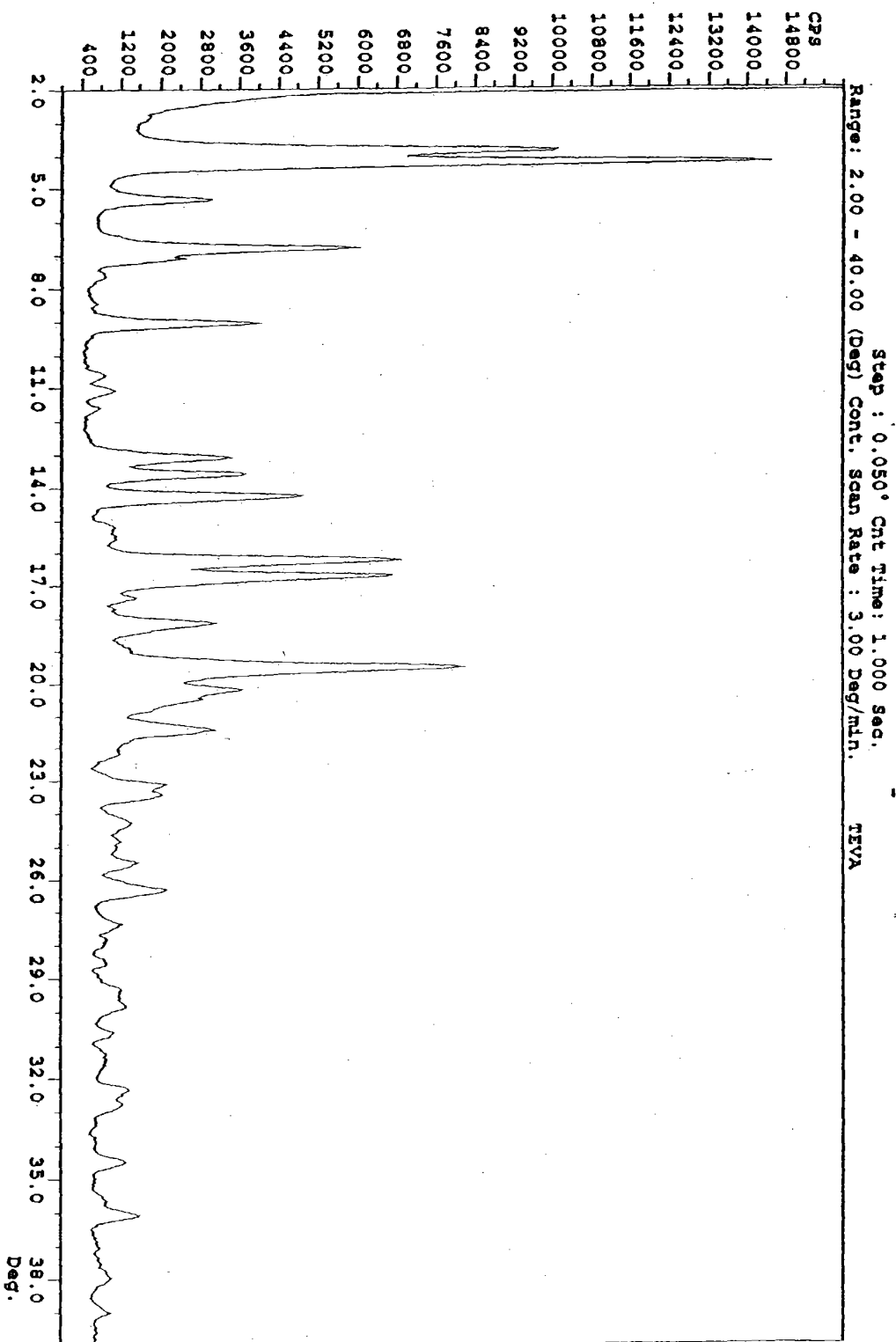


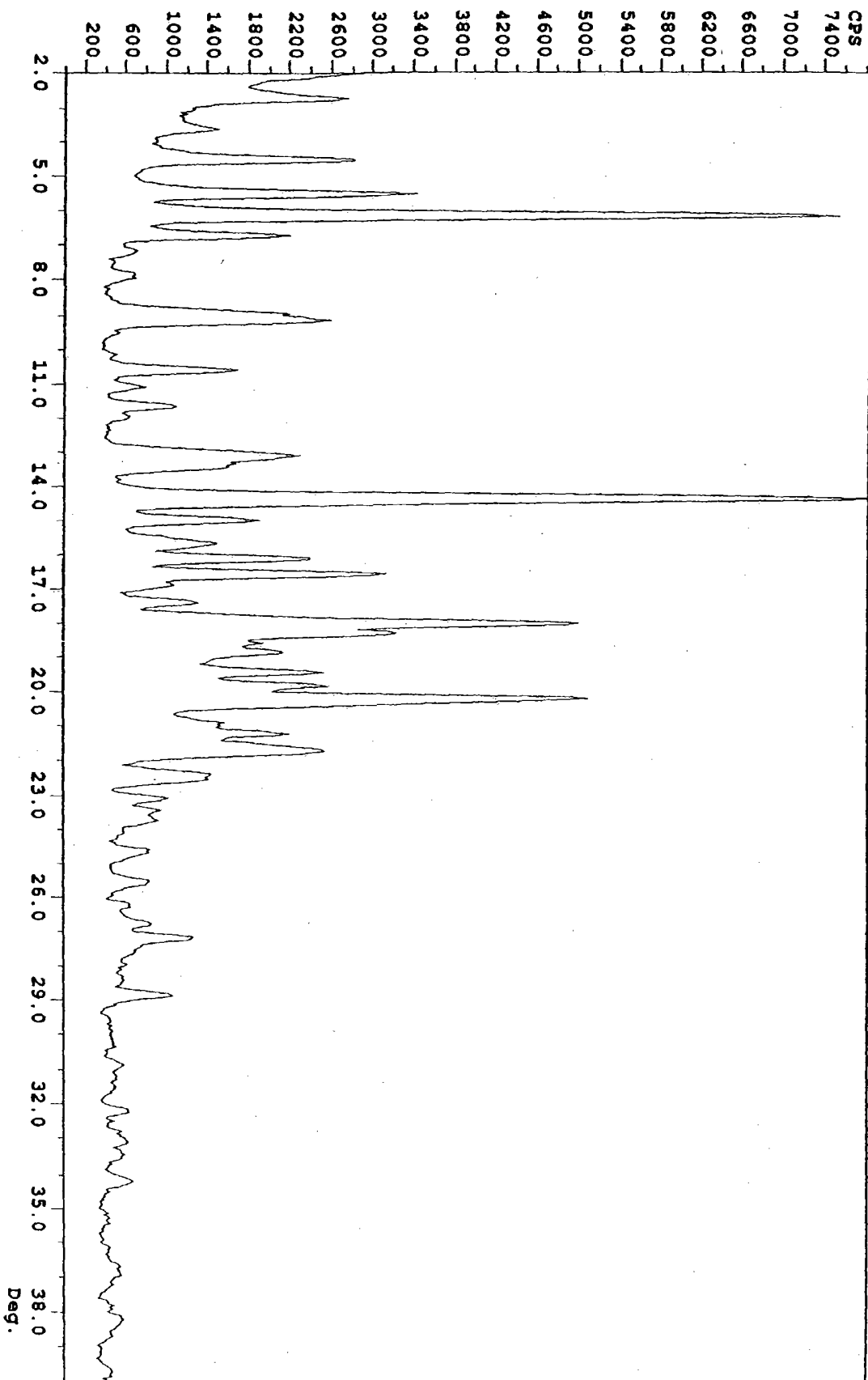
Fig 25
C



Sigma

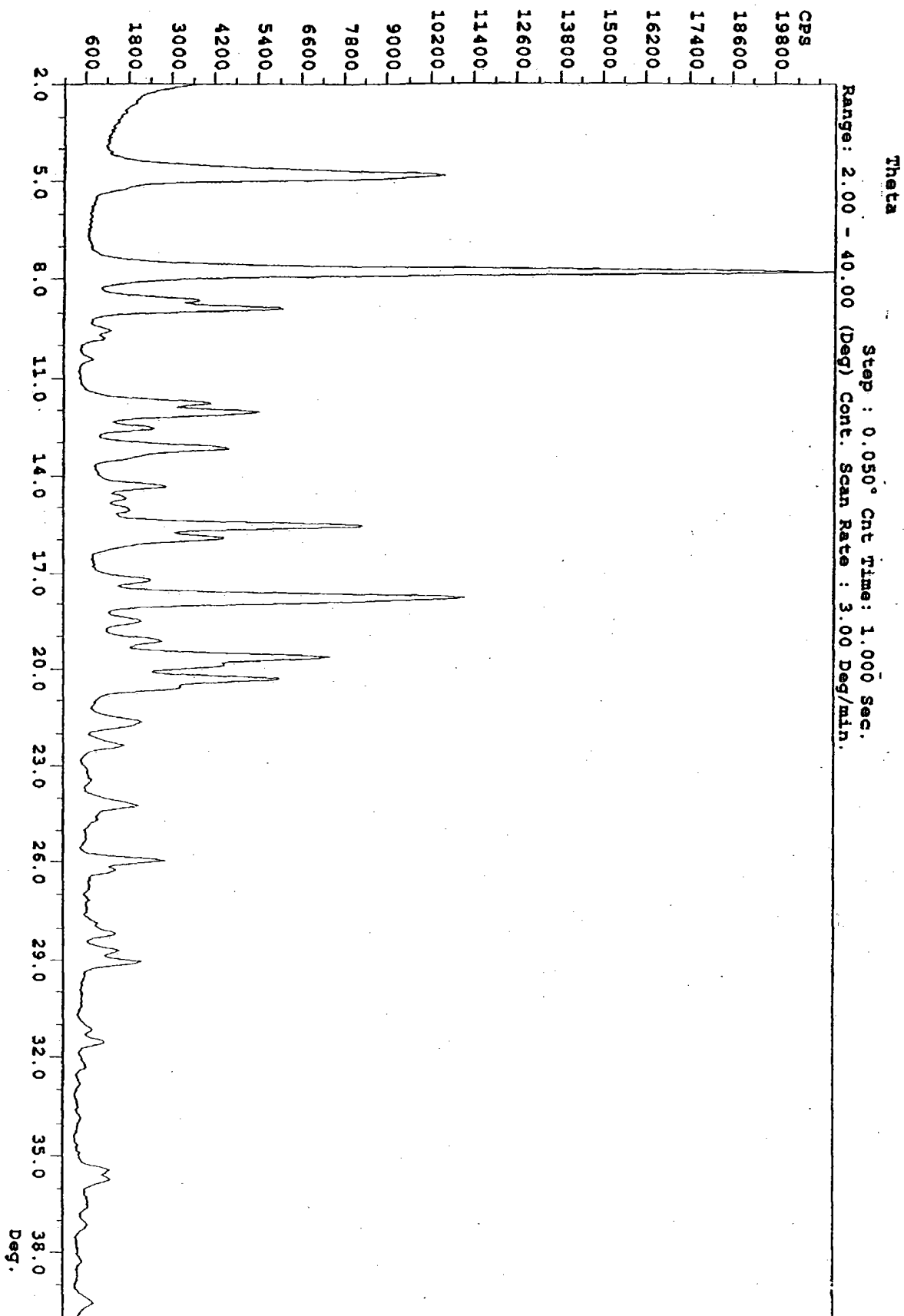
FIGURE 26

Step : 0.050° Cnt Time: 1.000 Sec.
Range: 2.00 - 40.00 (Deg) Cont. Scan Rate : 3.00 Deg/min.



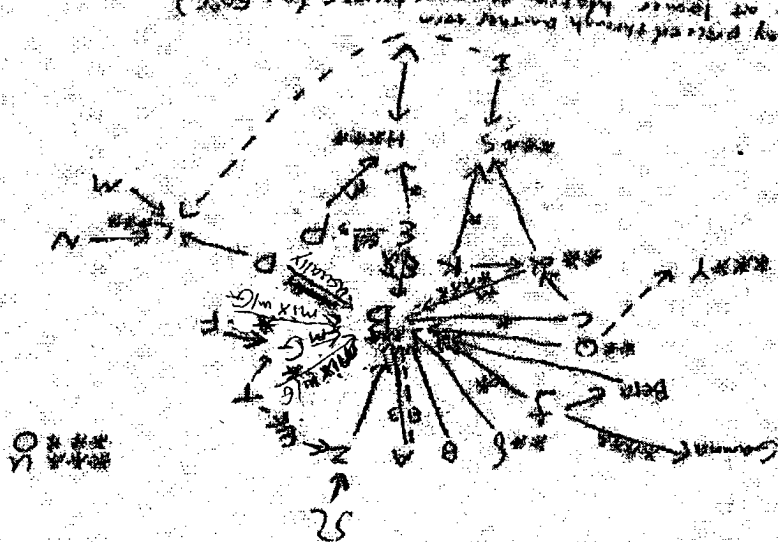
Form 2 (5)

FIGURE 27



Form 8

Figure 38 - Thermal stability chart



Transformation may proceed through partial form
 as thermally stable at lower heating temperatures (in 50°C)
 as thermally stable forms
 → Transformation of form storage of room temperature
 m with starting form.
 *** When starting material contains seeds.
 Results might vary depending on the solvents of form Epurion used.

FIGURE 29
Form 2

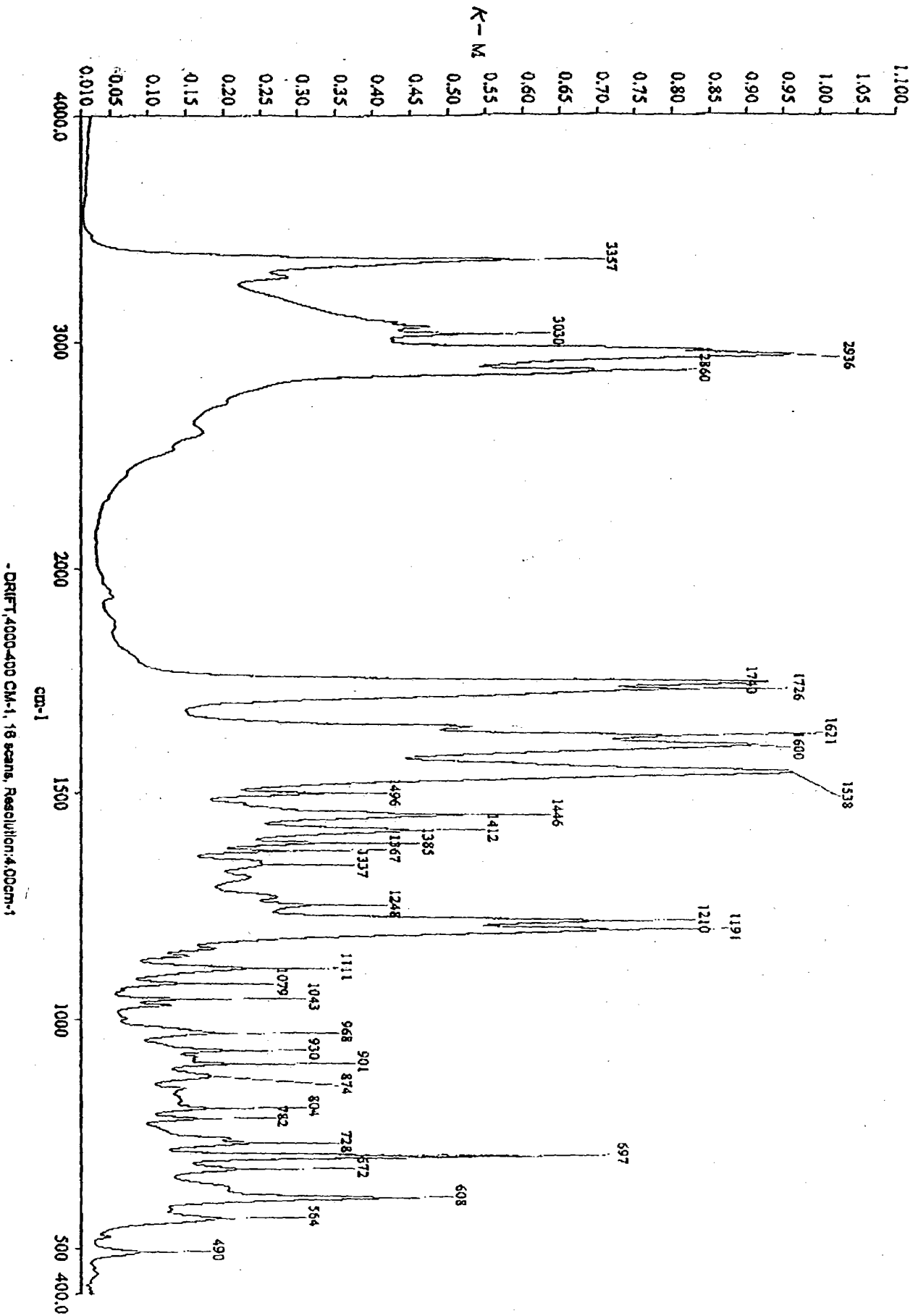


FIGURE 30
Form P

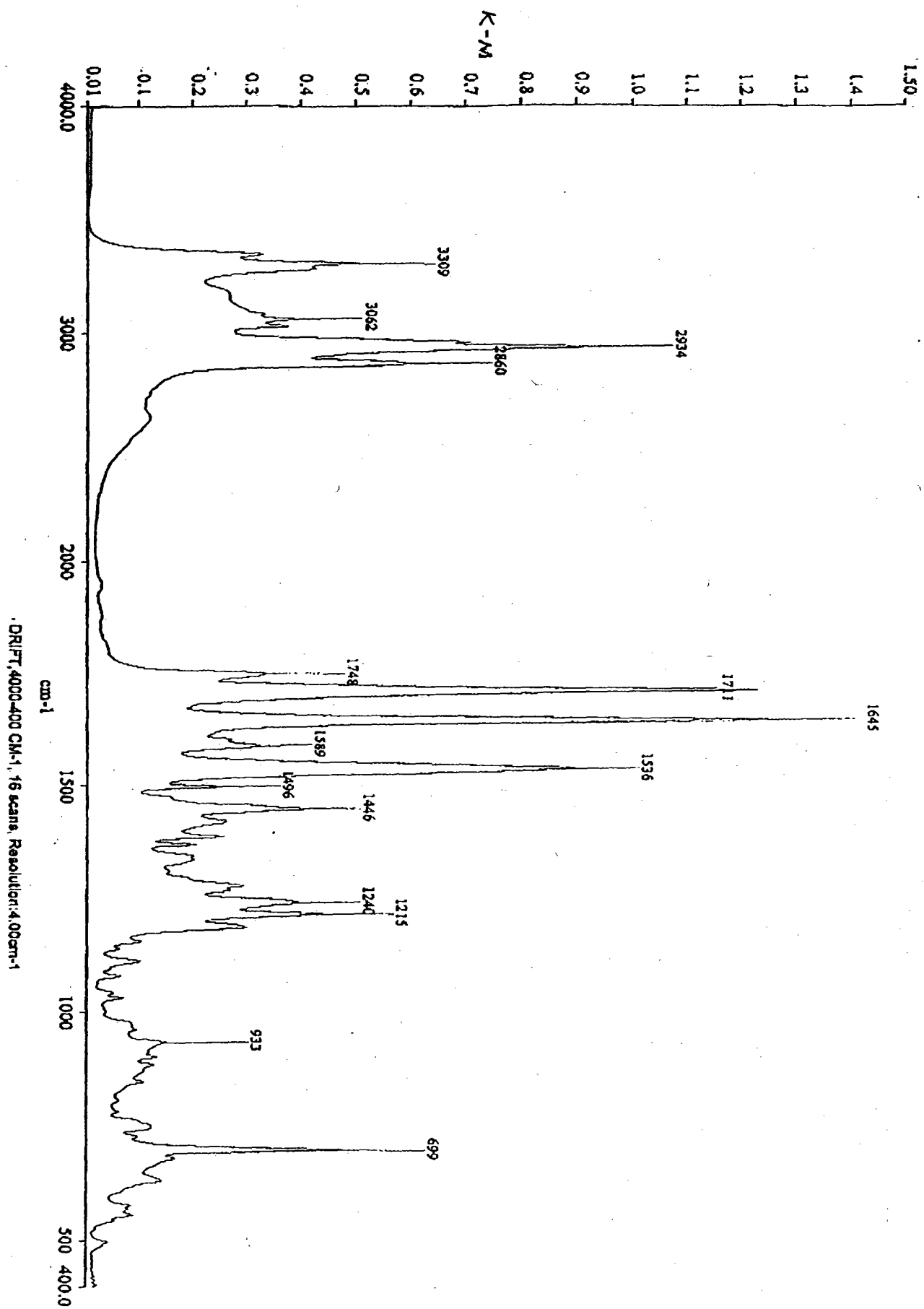


FIGURE 30
Form U

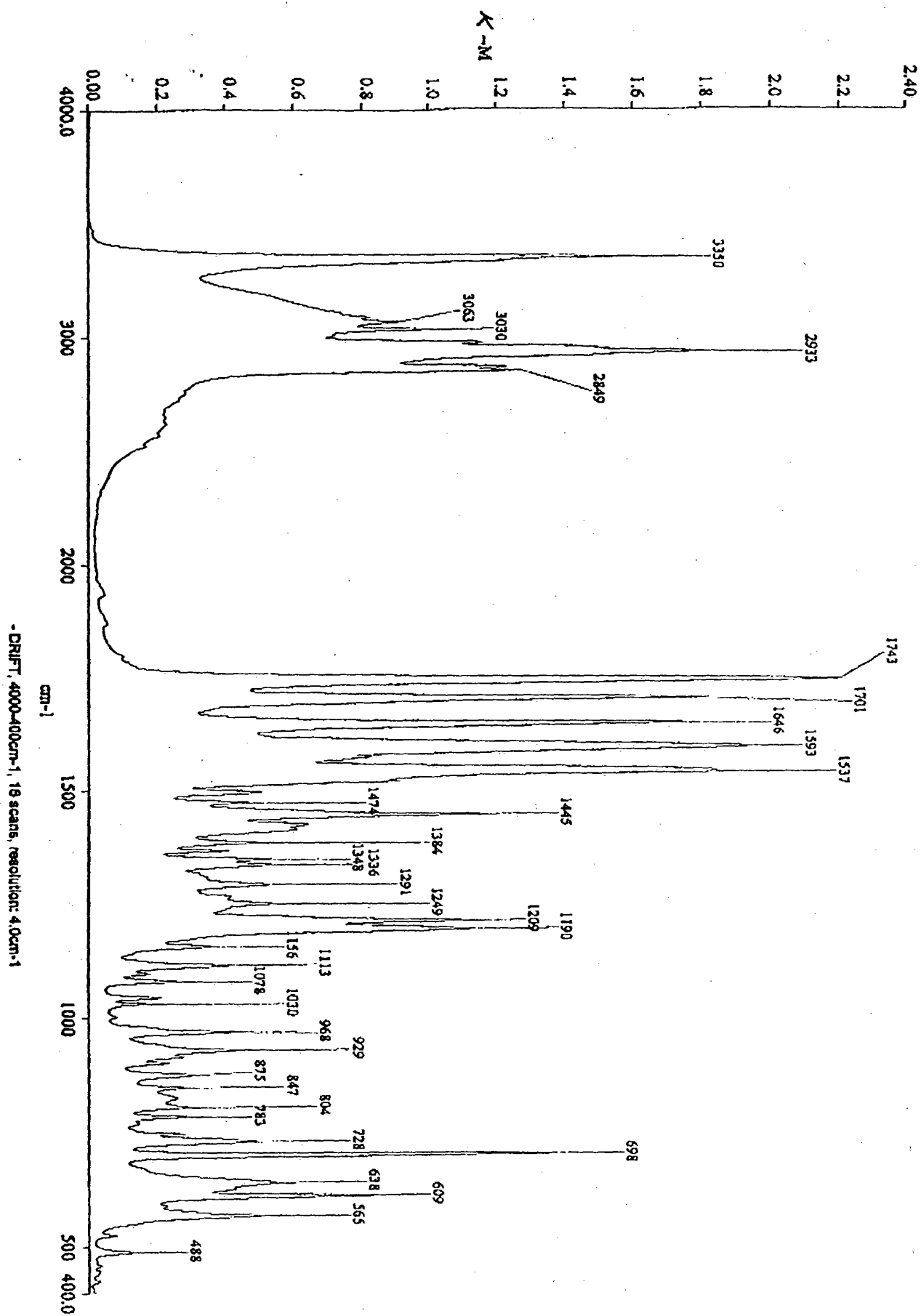


Figure ~~32~~ ³² - Nataglinide Form Z

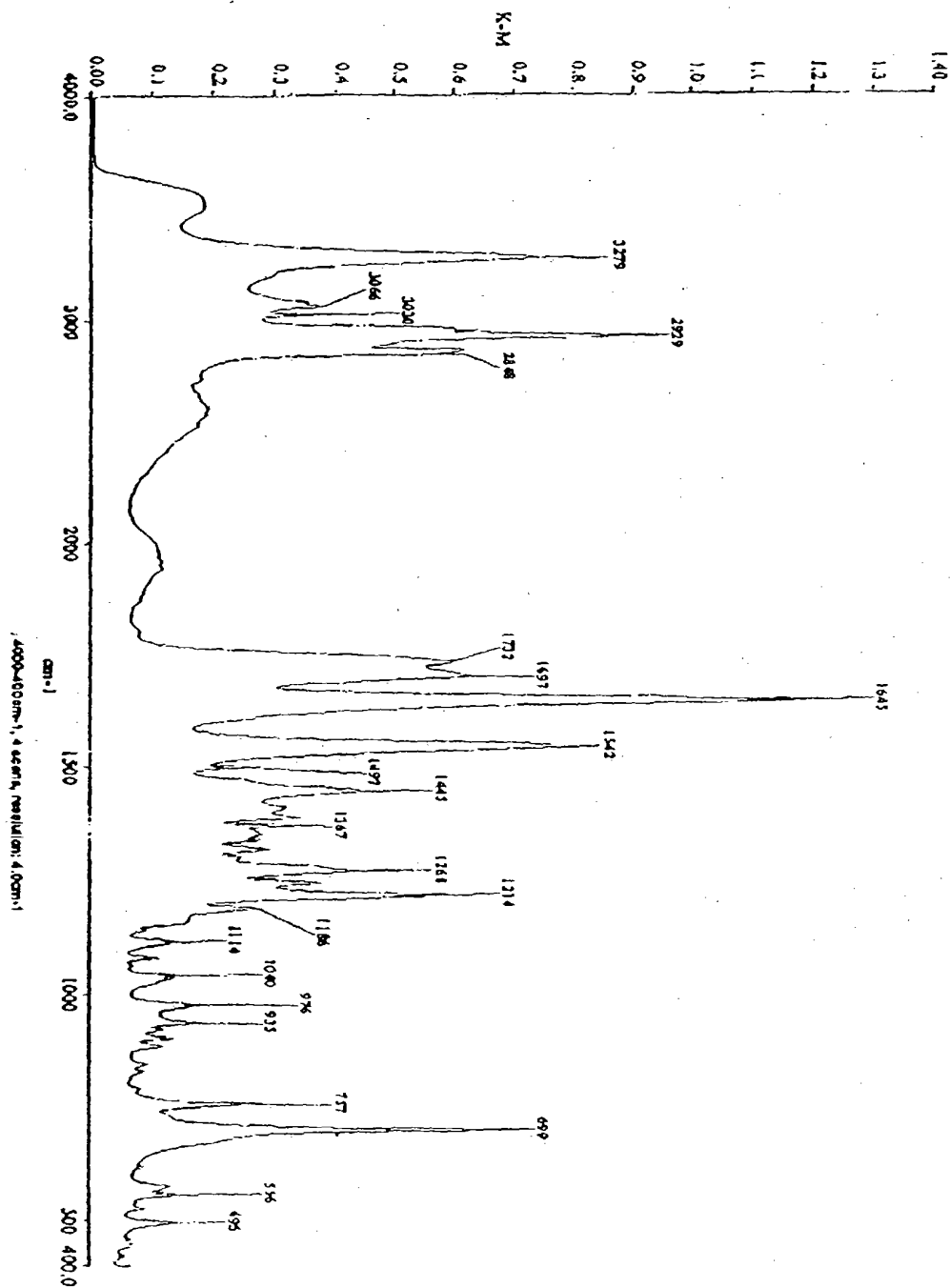


Figure 33
Form A

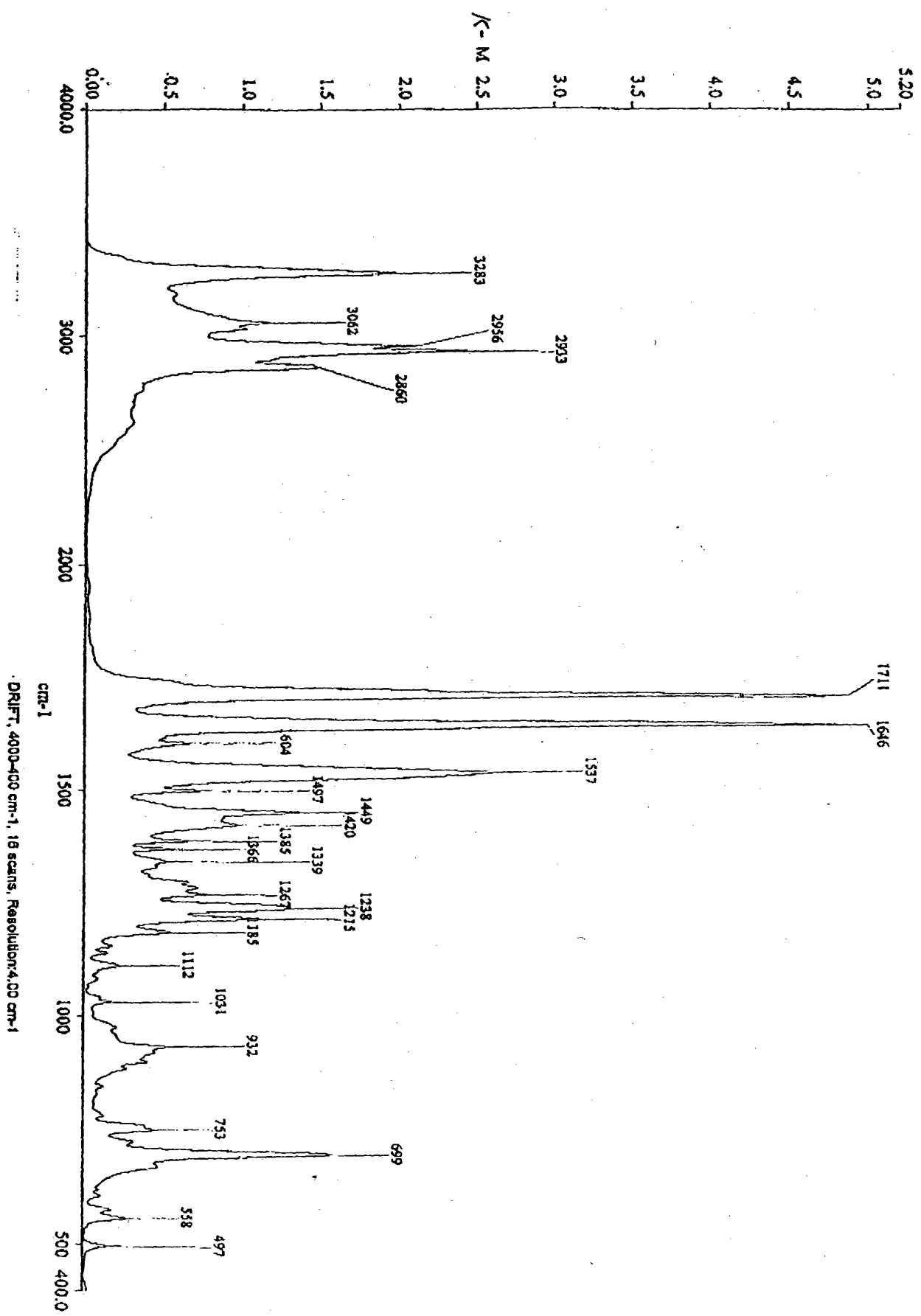


Figure 34 Form delta

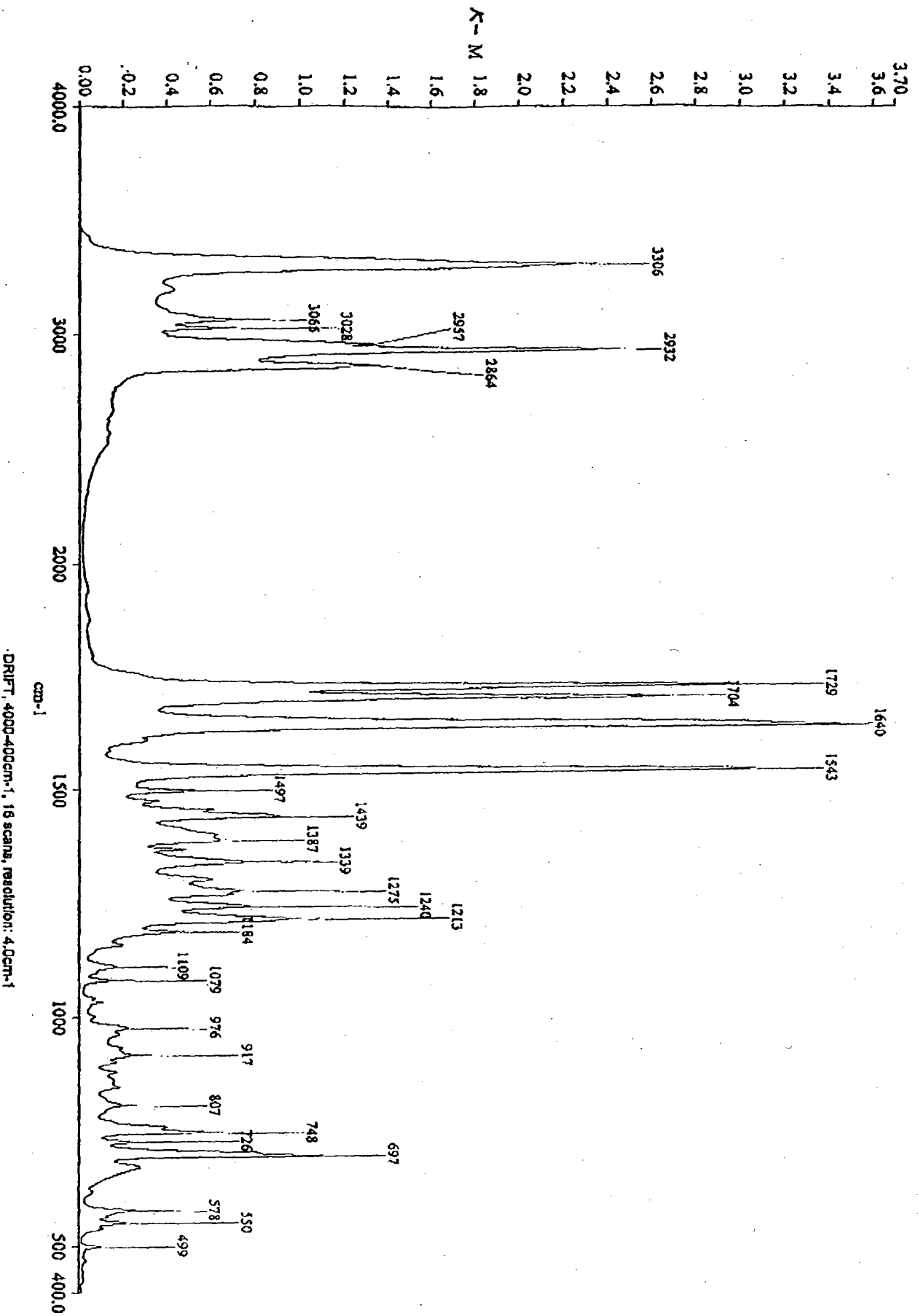
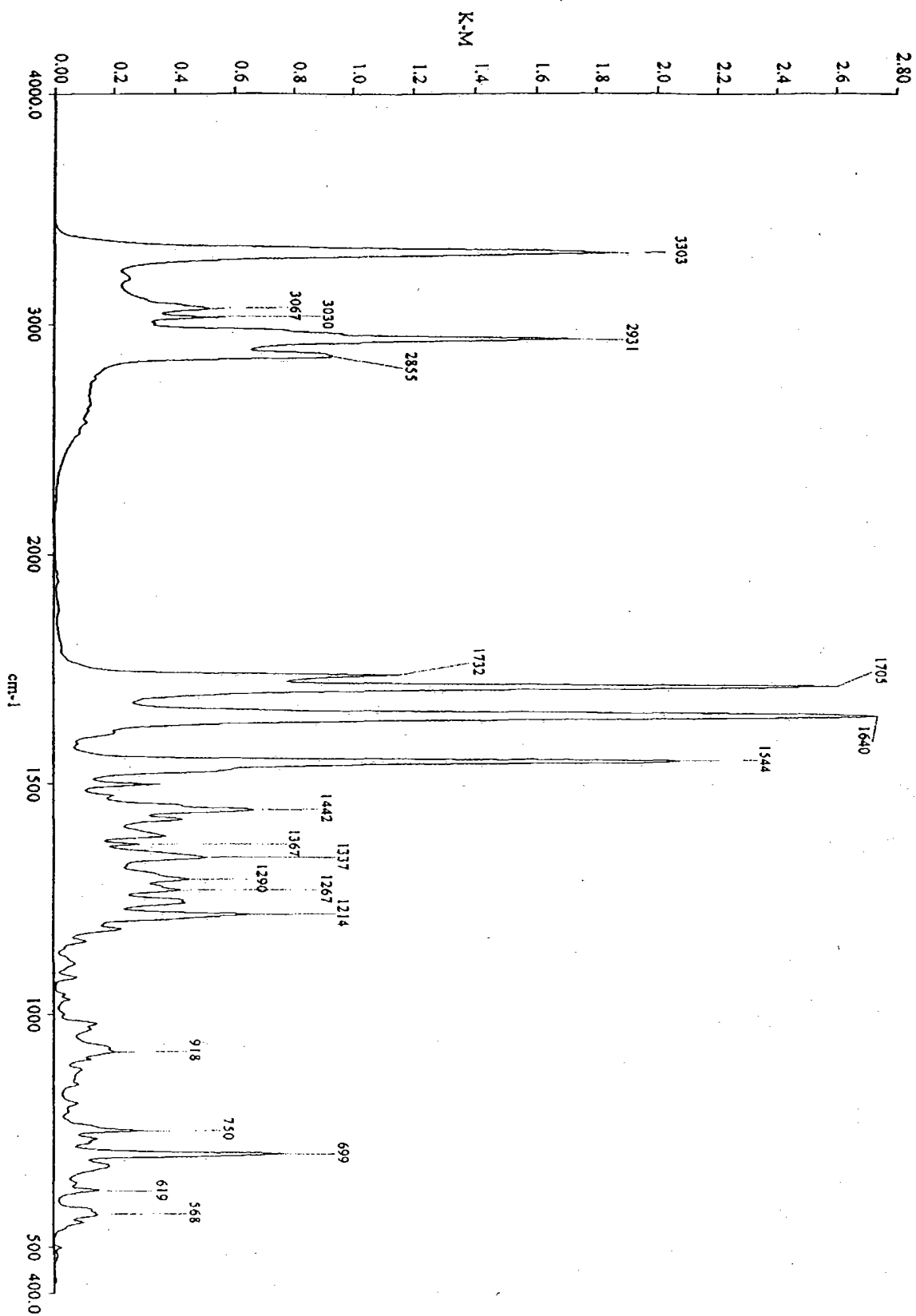


FIGURE 35

- Form 0



DRIFT, 4000-400CM-1, 16 SCANS RESOLUTION: 4.0CM-1

form 0 (0)

FIGURE 36
Form A

Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min

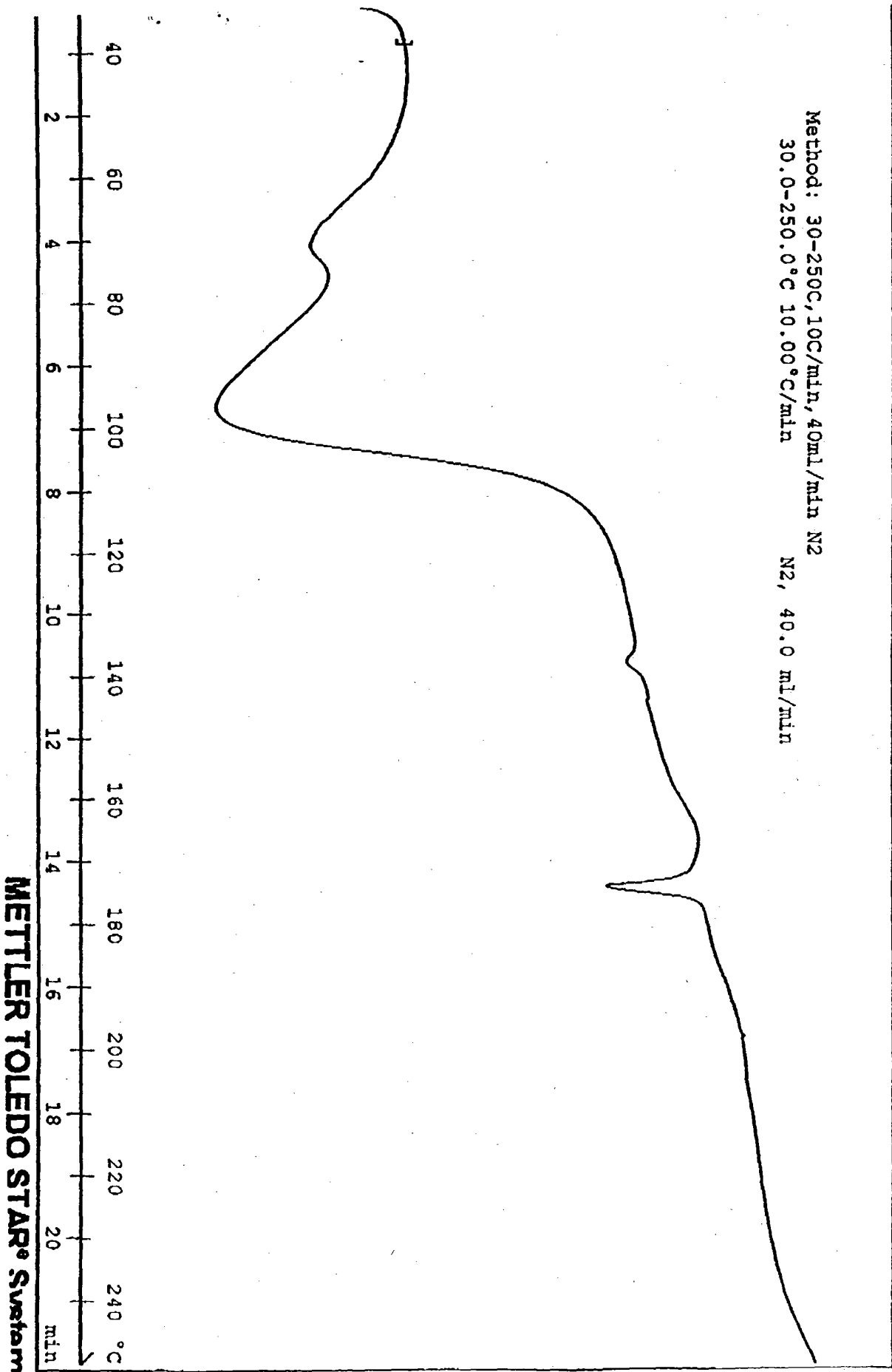


FIGURE 39 Form D

Method: 30-250°C, 10°C/min, 40ml/min N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min

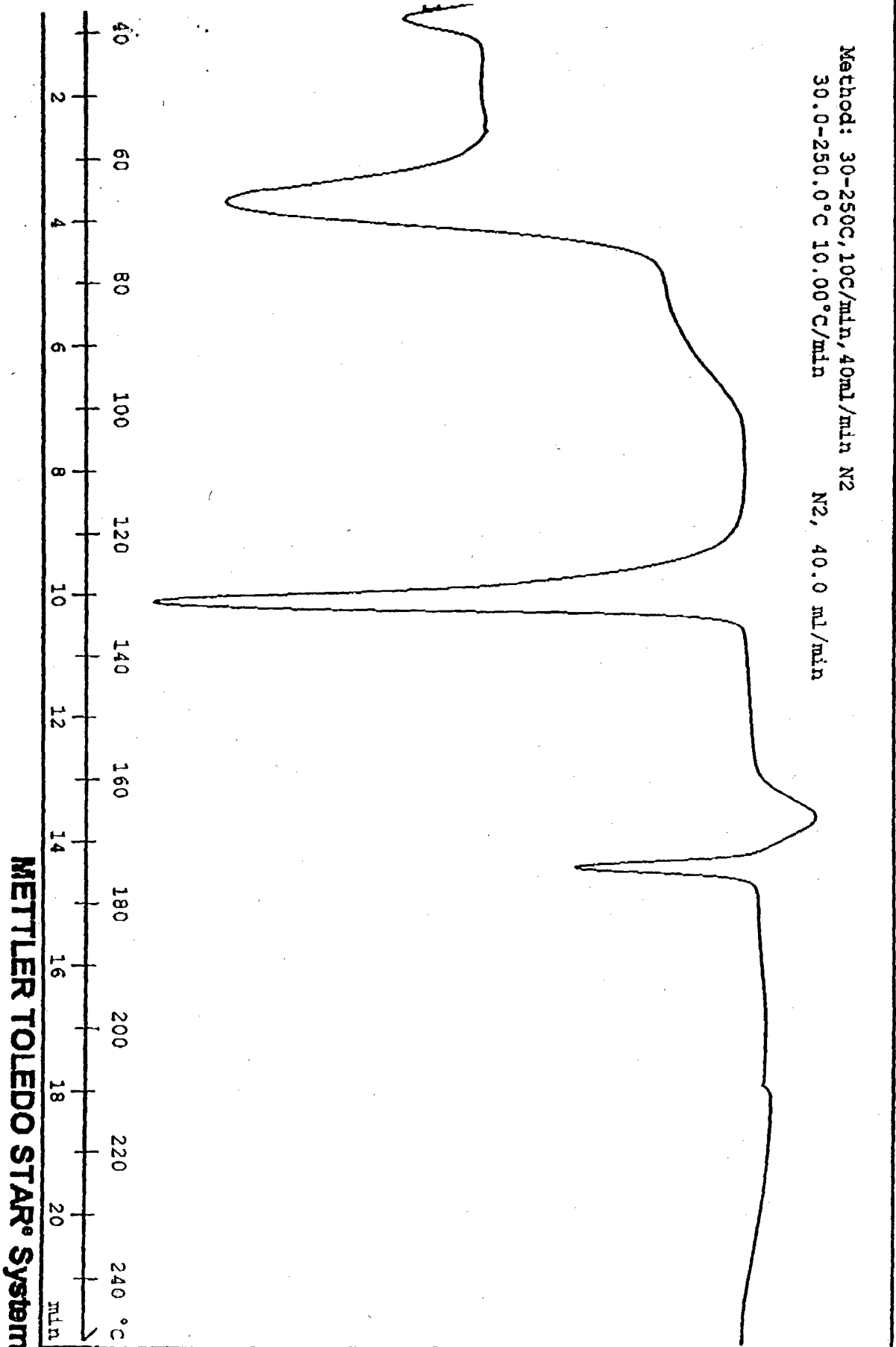


FIGURE 38

Form E

Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min

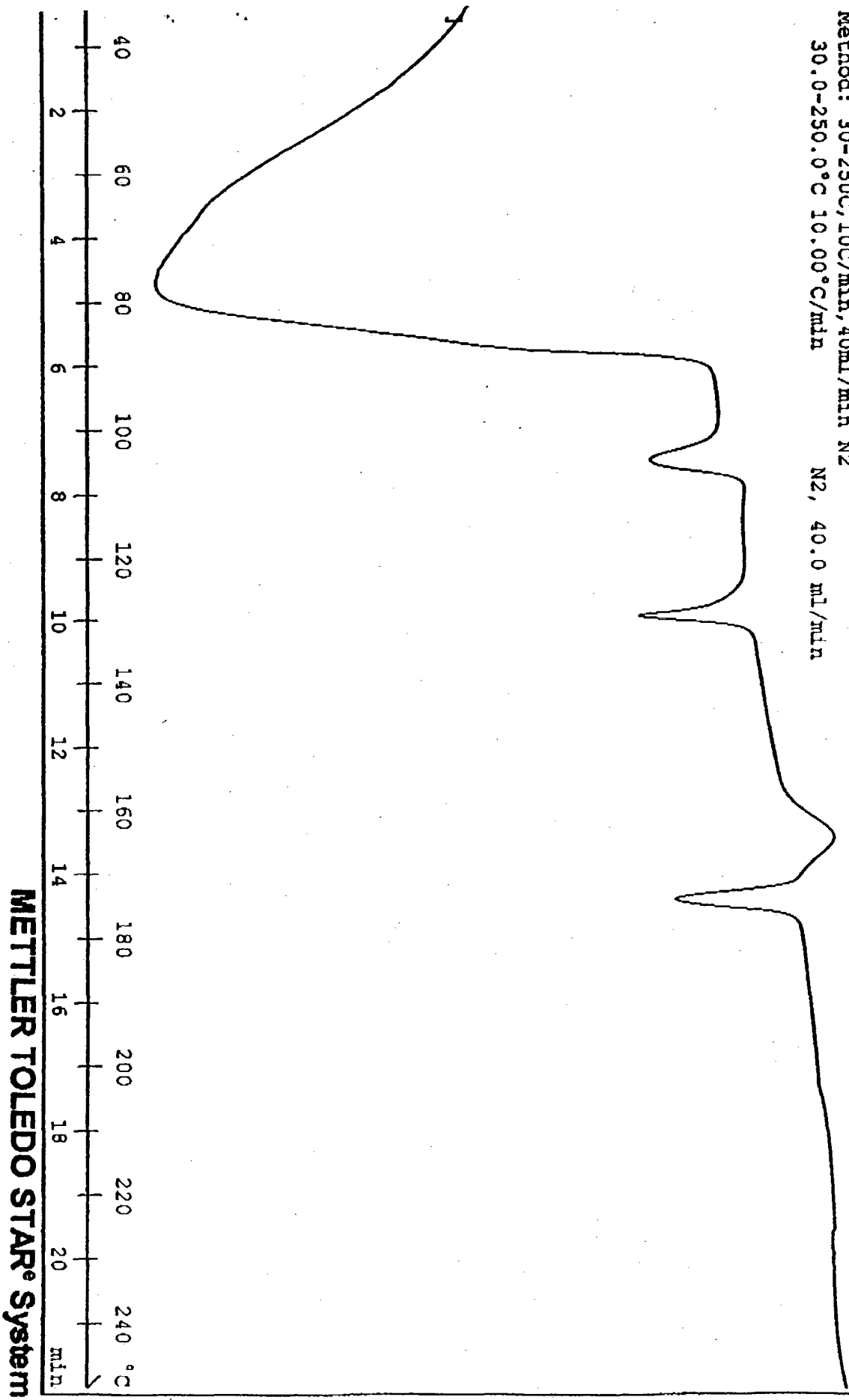
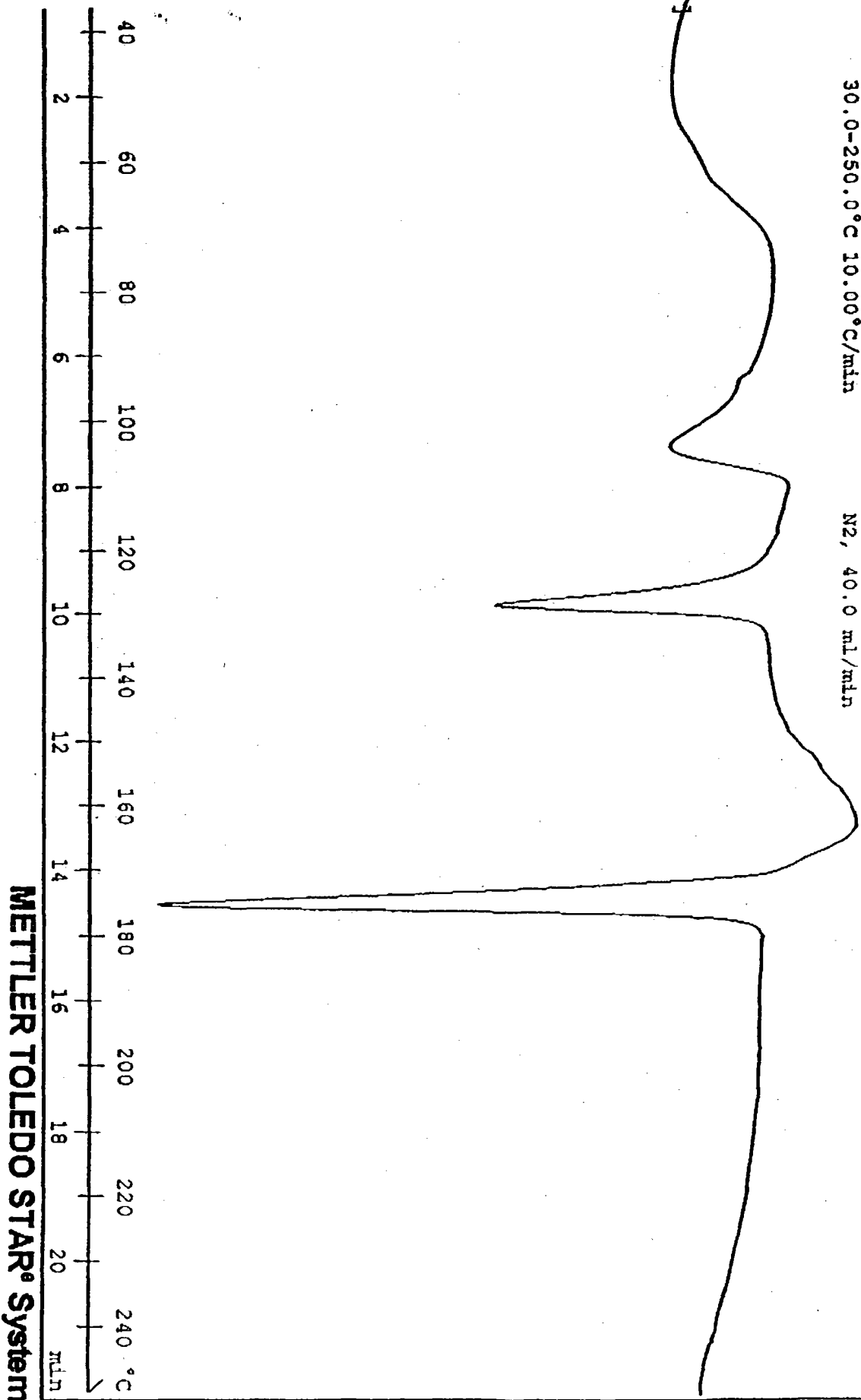


FIGURE 29

Method: 30-250C, 10C/min, 40ml/min, N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min



40
FIGURE 08

Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min

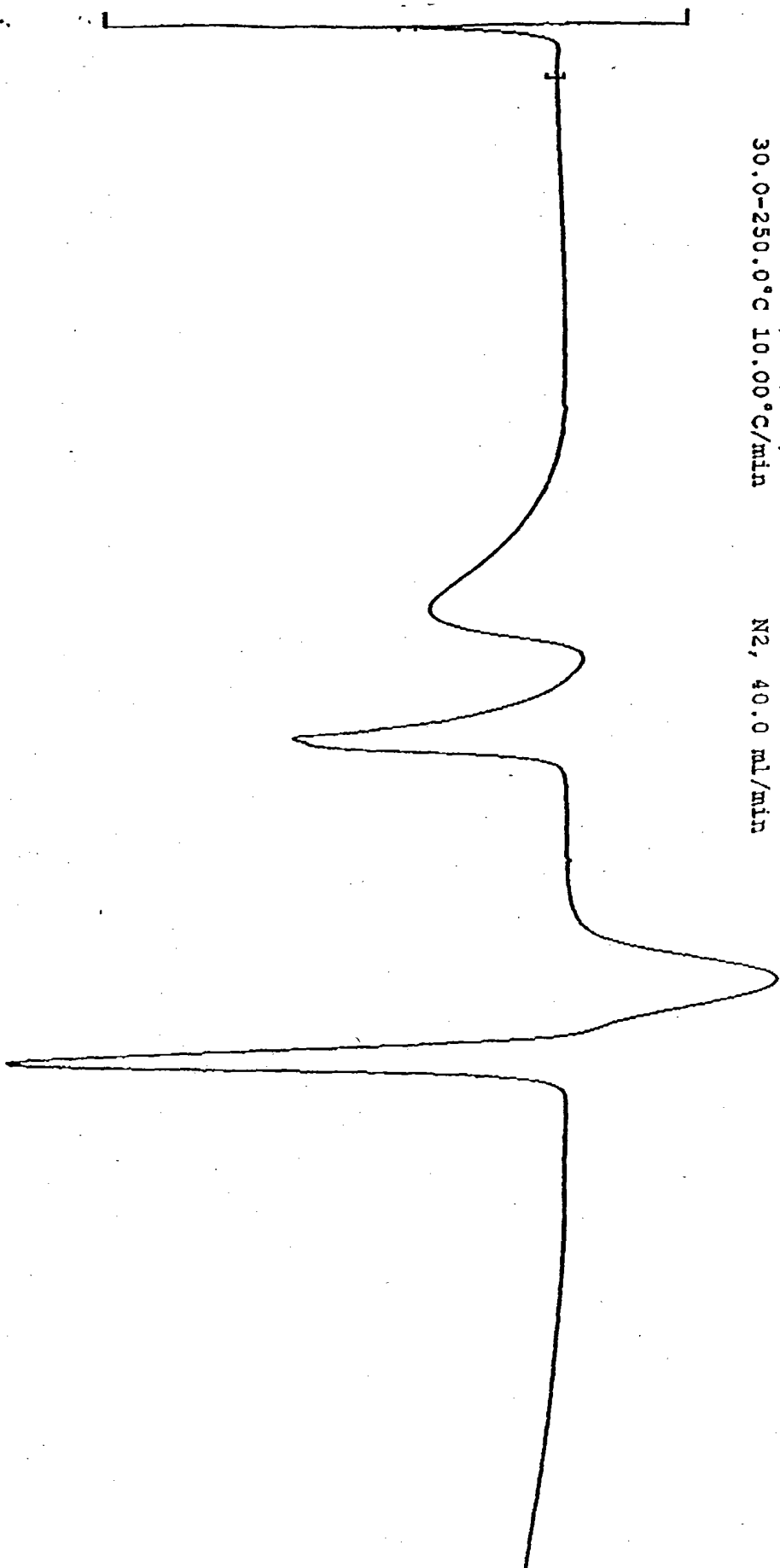
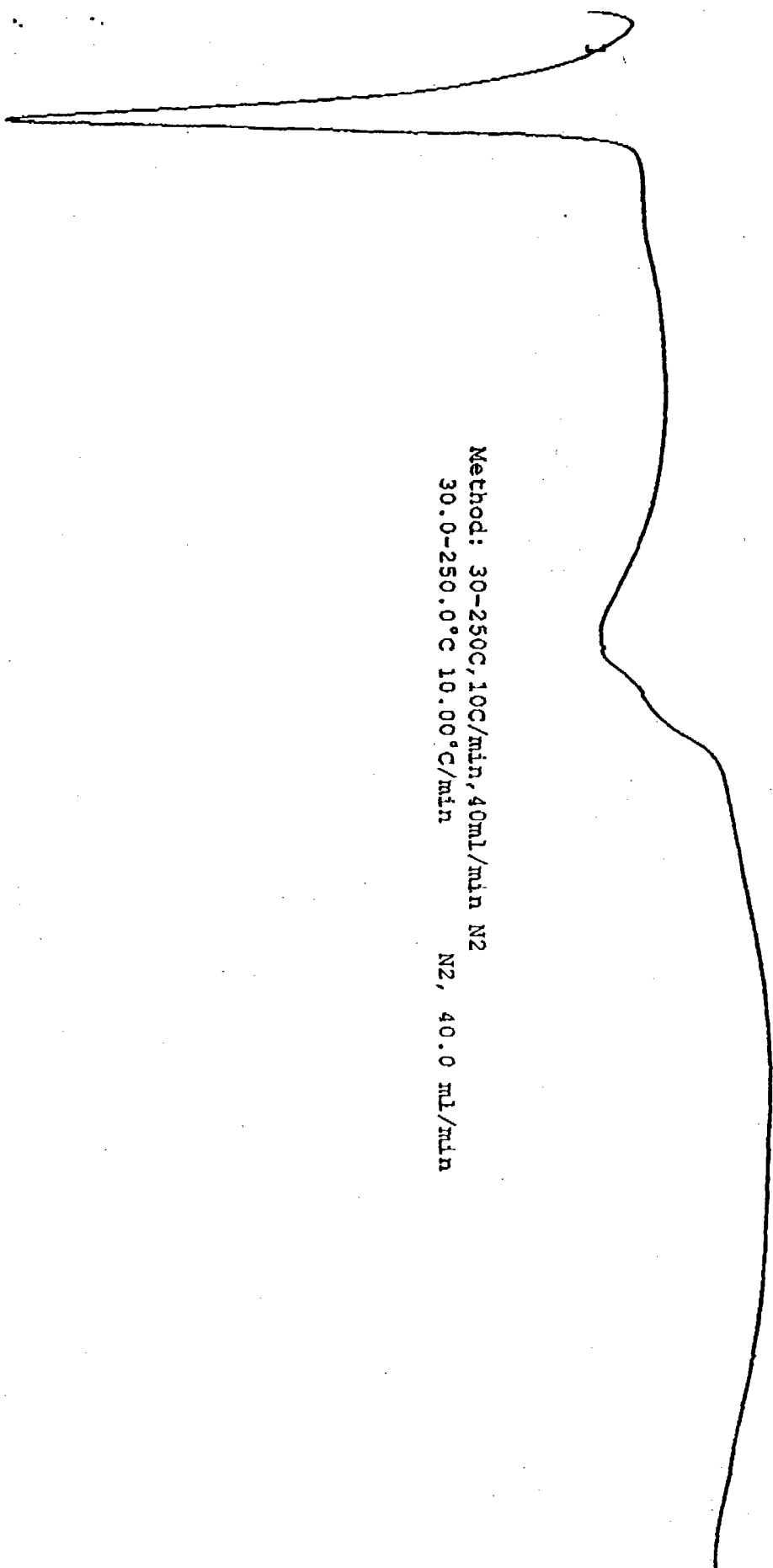


FIGURE 91

Form I



METTLER TOLEDO STAR® System

FIGURE 4a
Form J

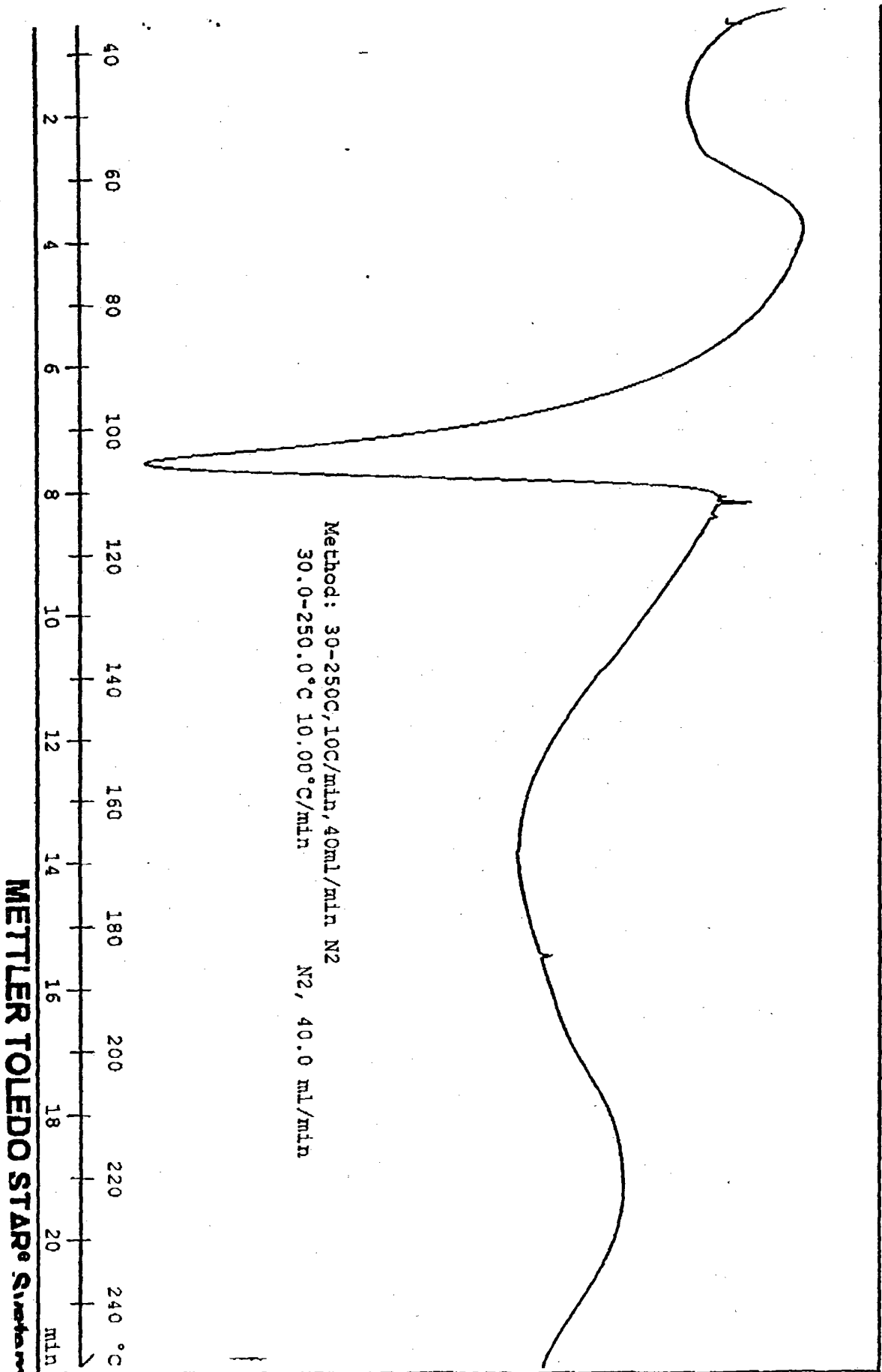


FIGURE 4/3
Form K

Method: 30-250°C, 100 ml/min, 40 ml/min N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min

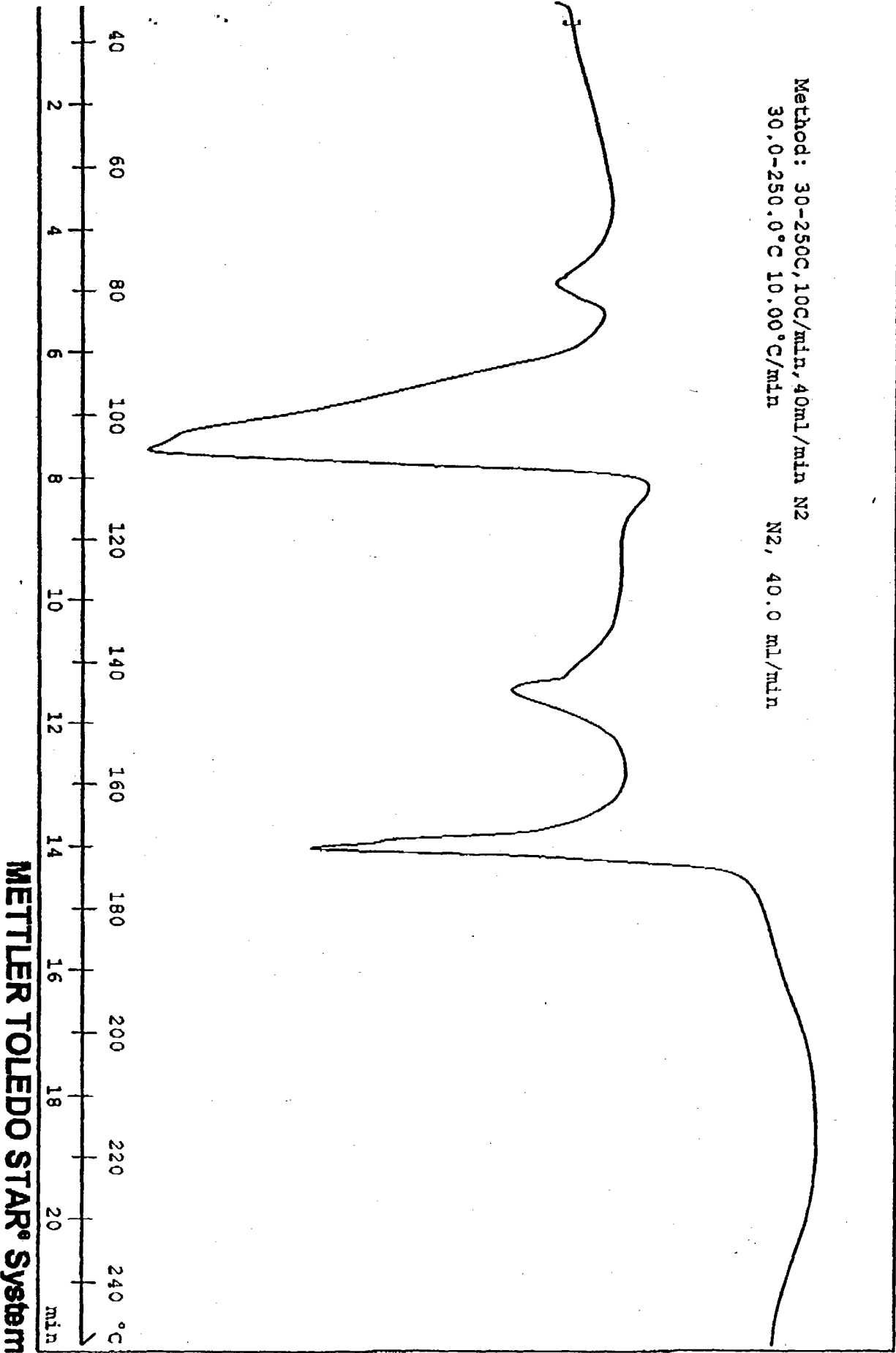


FIGURE 42
4/4
Form L

Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min

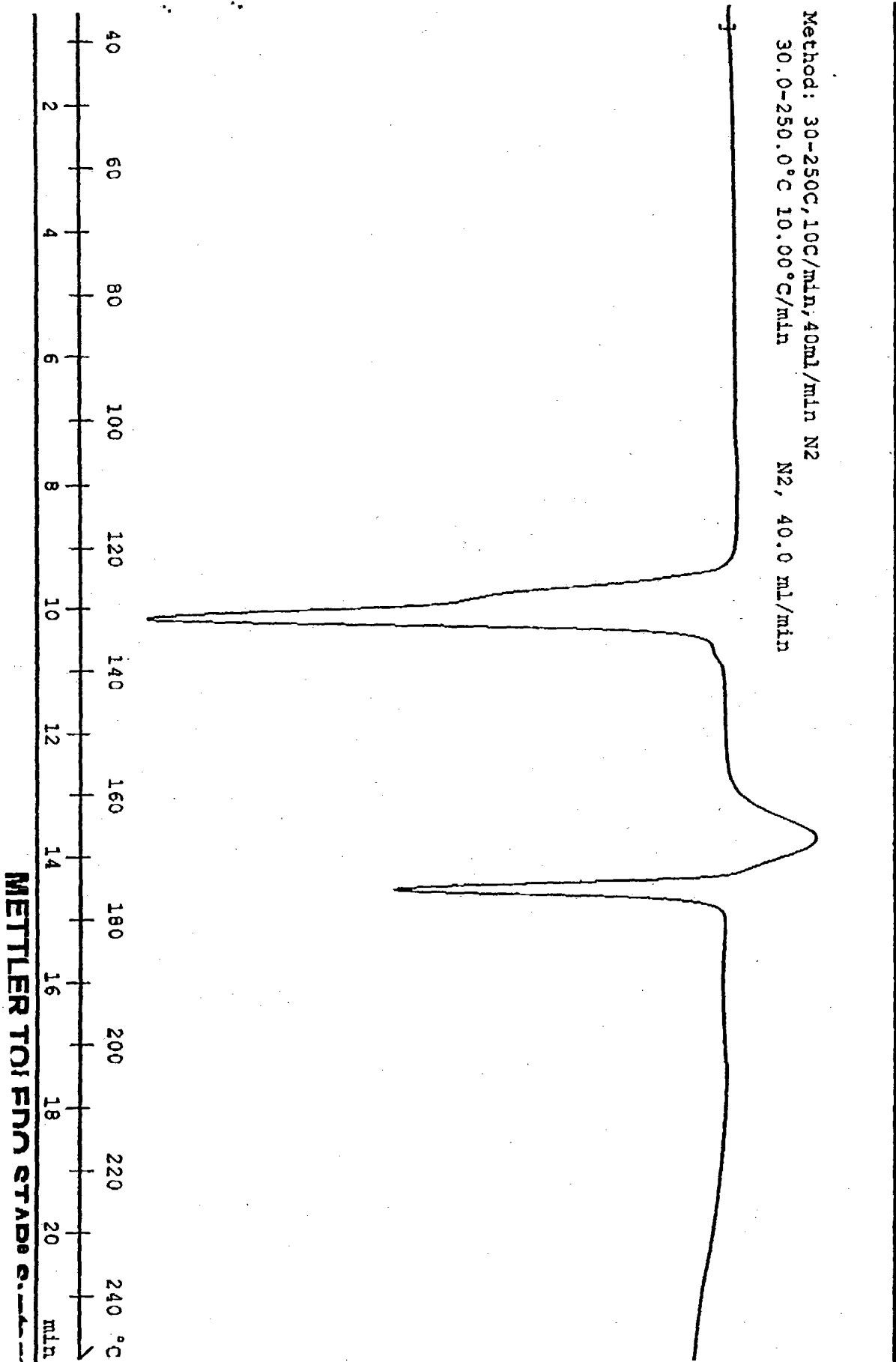
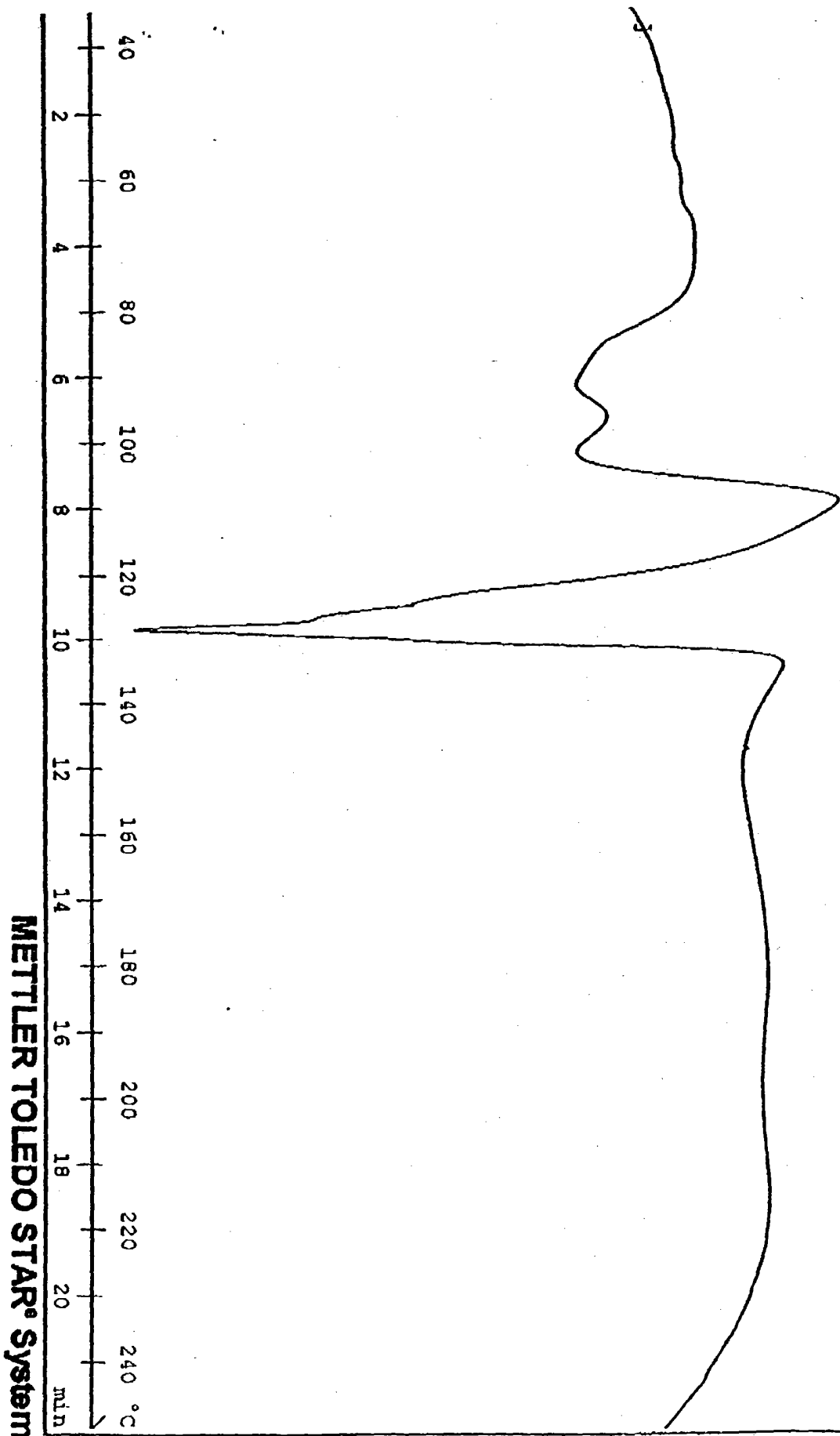


Figure 45
Form N

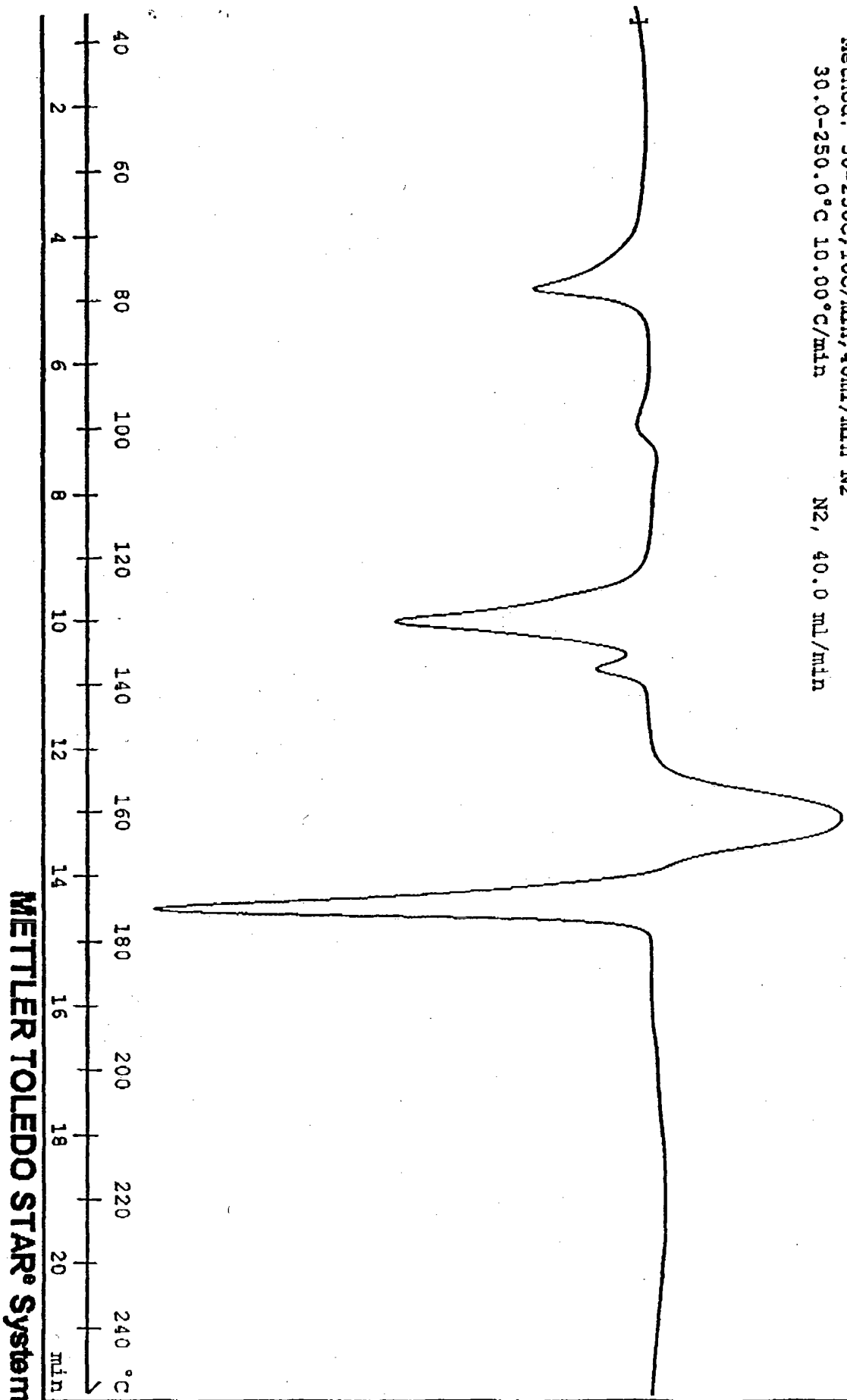
Method: 30-250°C, 10°C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 mL/min



METTLER TOLEDO STAR® System

FIGURE 44
Form N

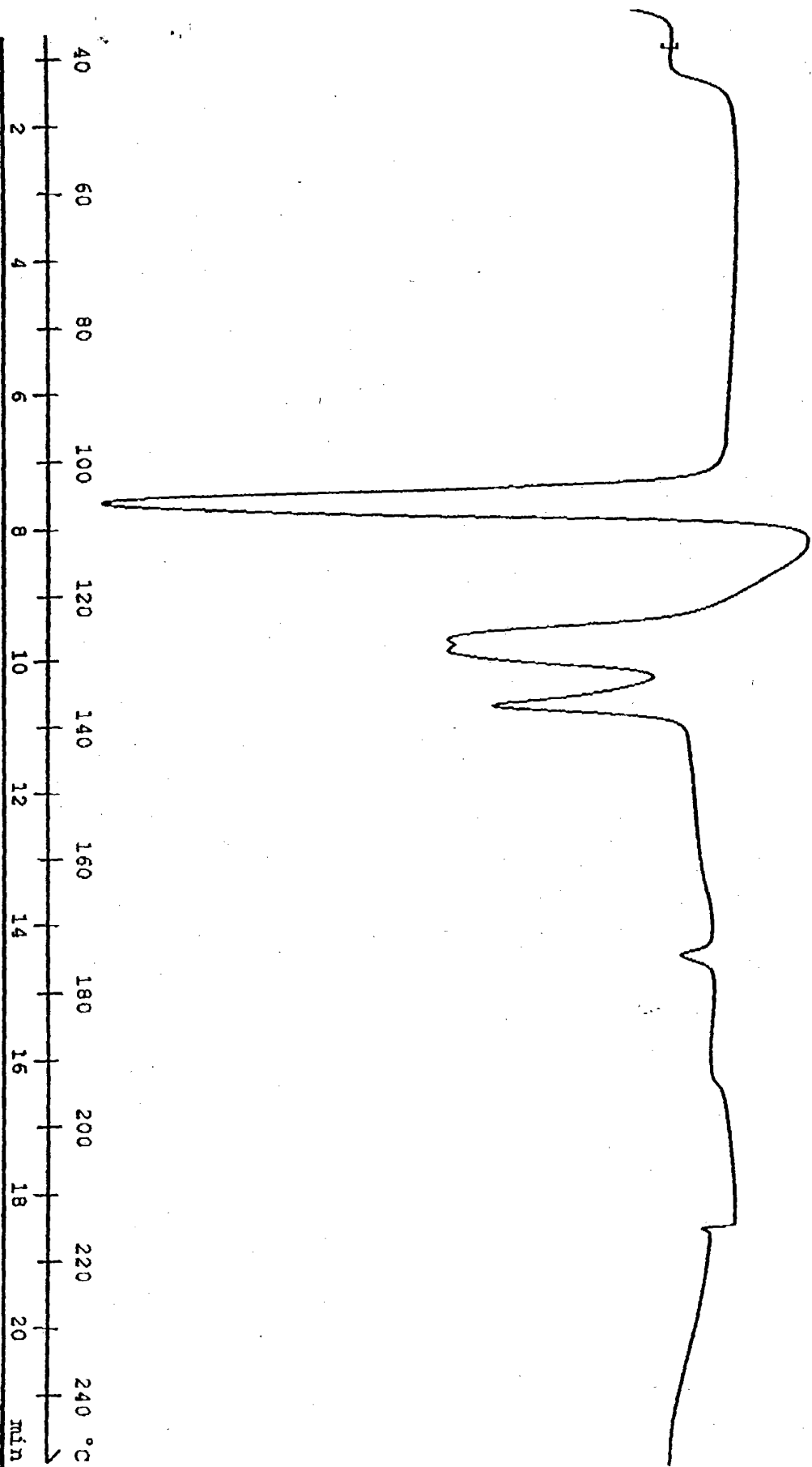
Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® System

FIGURE #5 47
Form C

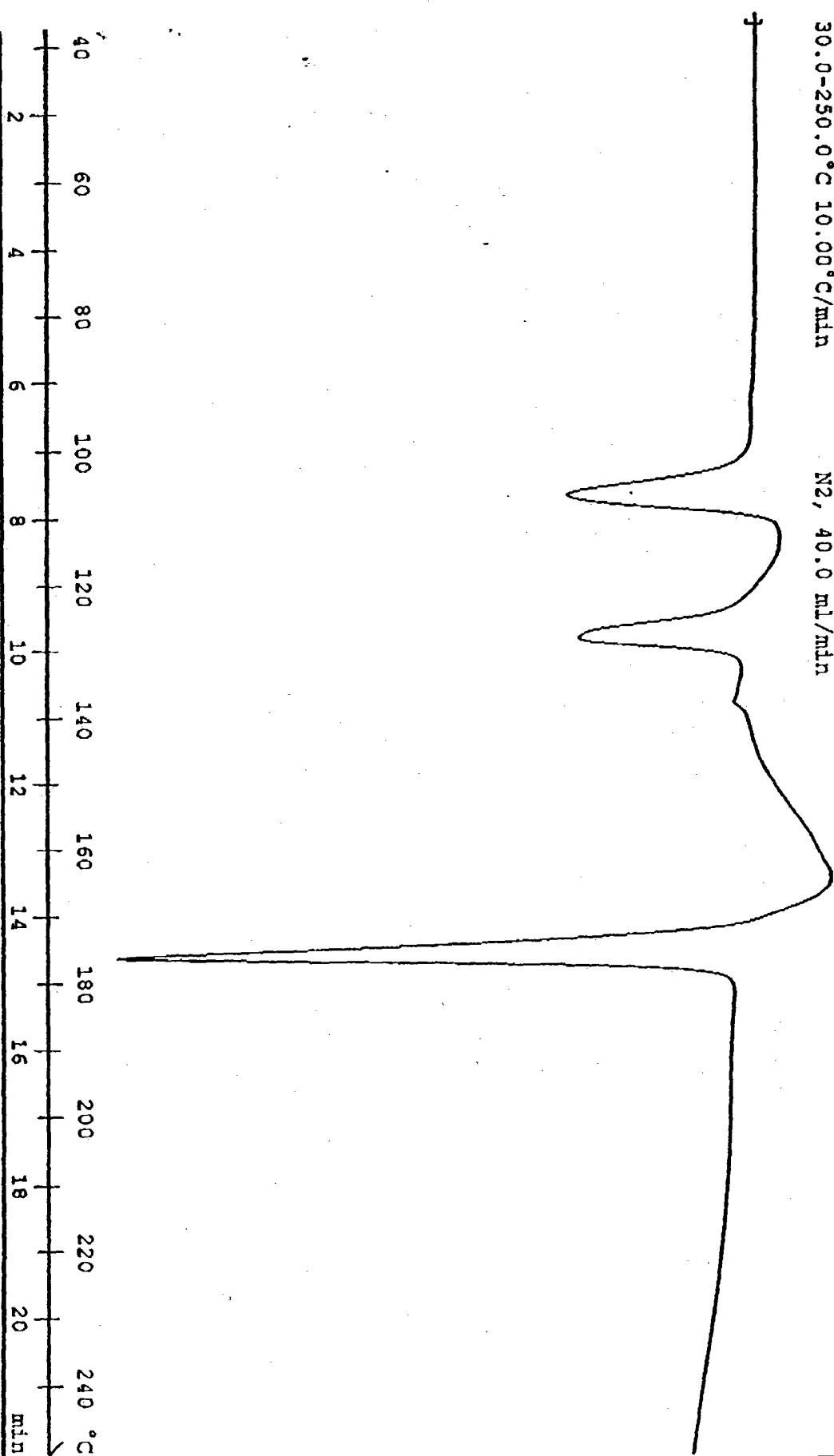
Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAB. C.

FIGURE 48
Form P

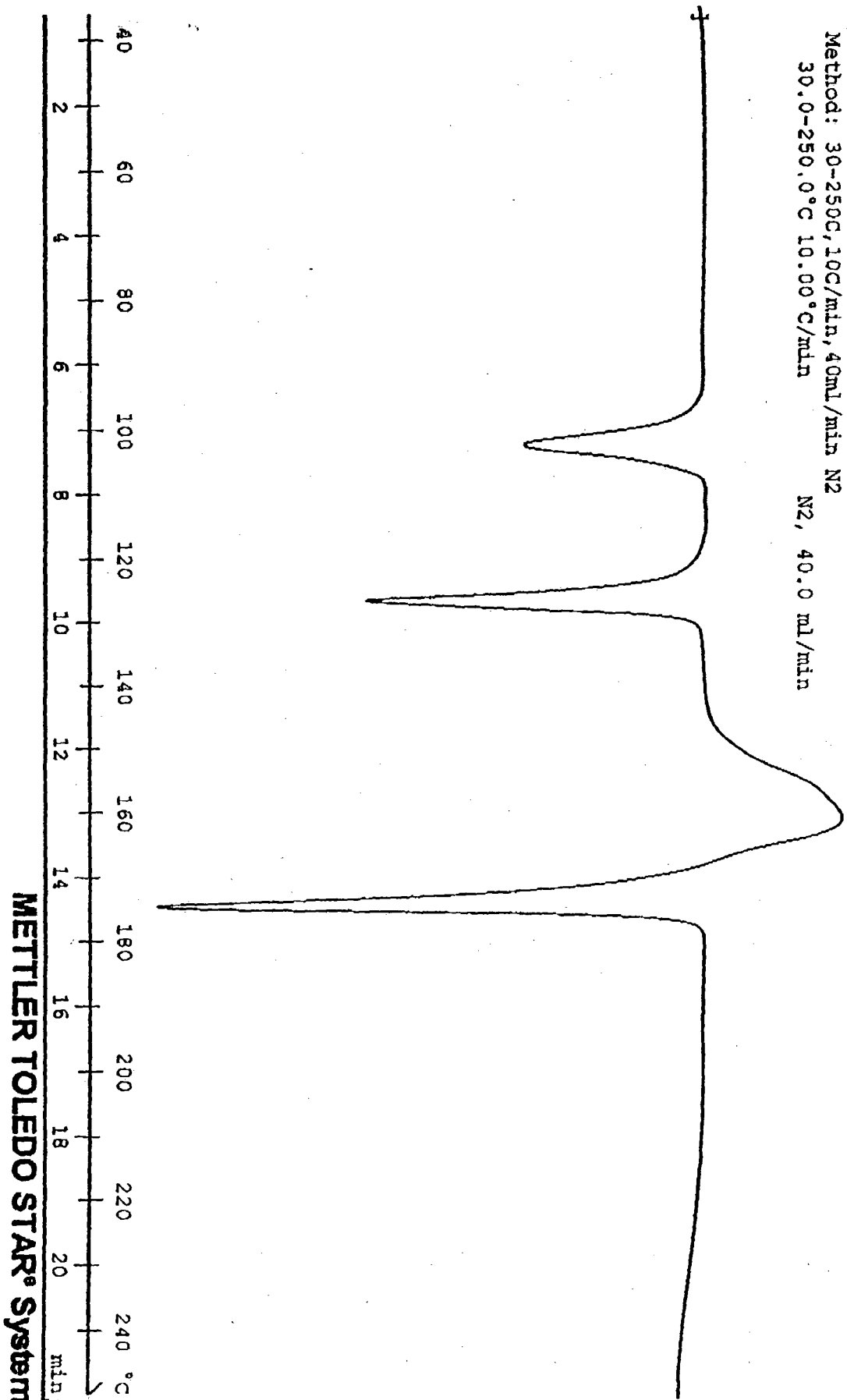
Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® System

FIGURE 49
Form Q

Method: 30-250°C, 100°C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® System

FIGURE 48-50
Form T

Method: 30-250°C, 10°C/min, 40ml/min N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min

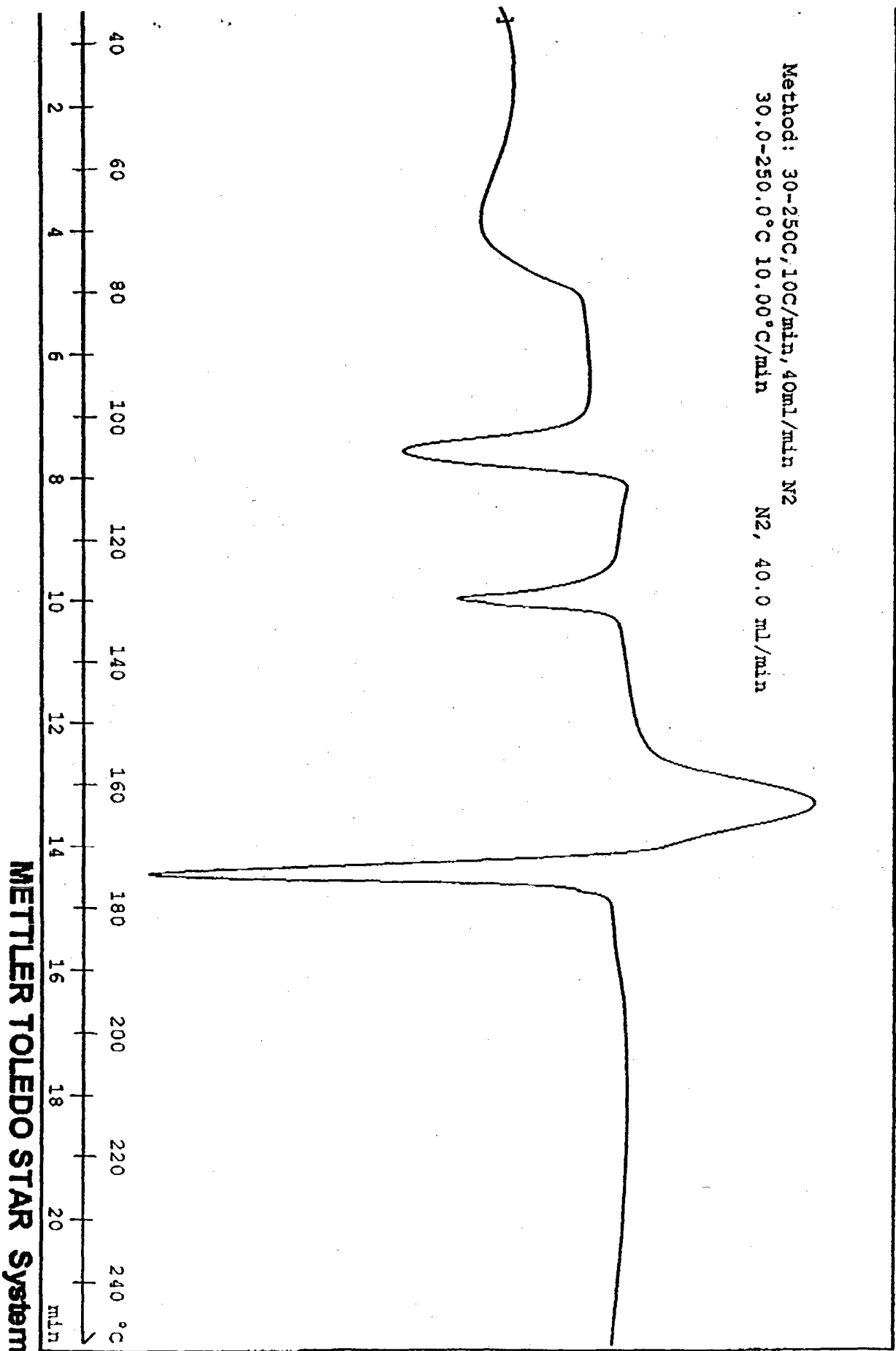
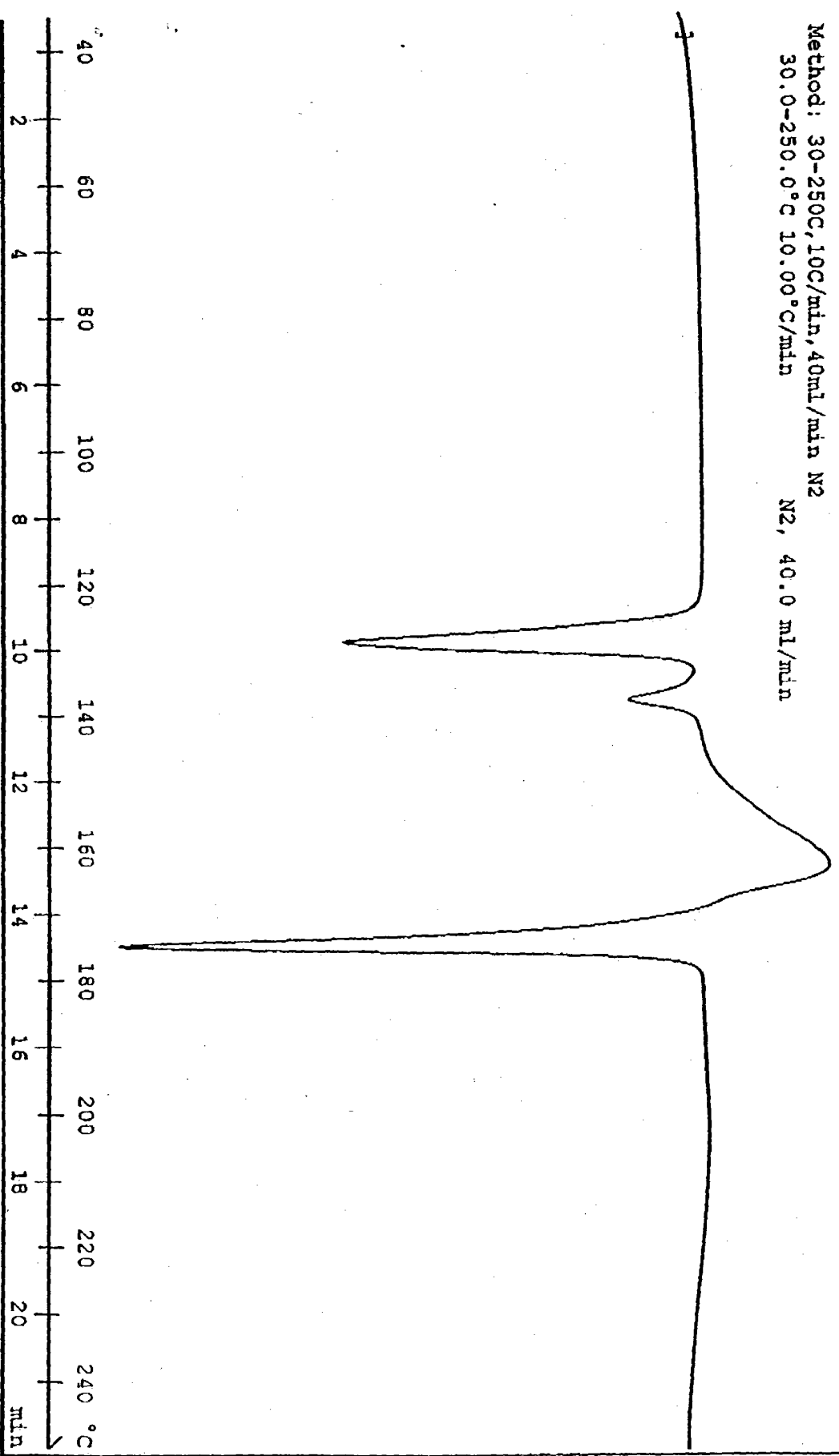


FIGURE 49. 51
Form 1A

Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR System

FIGURE 5a
Form V

Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min

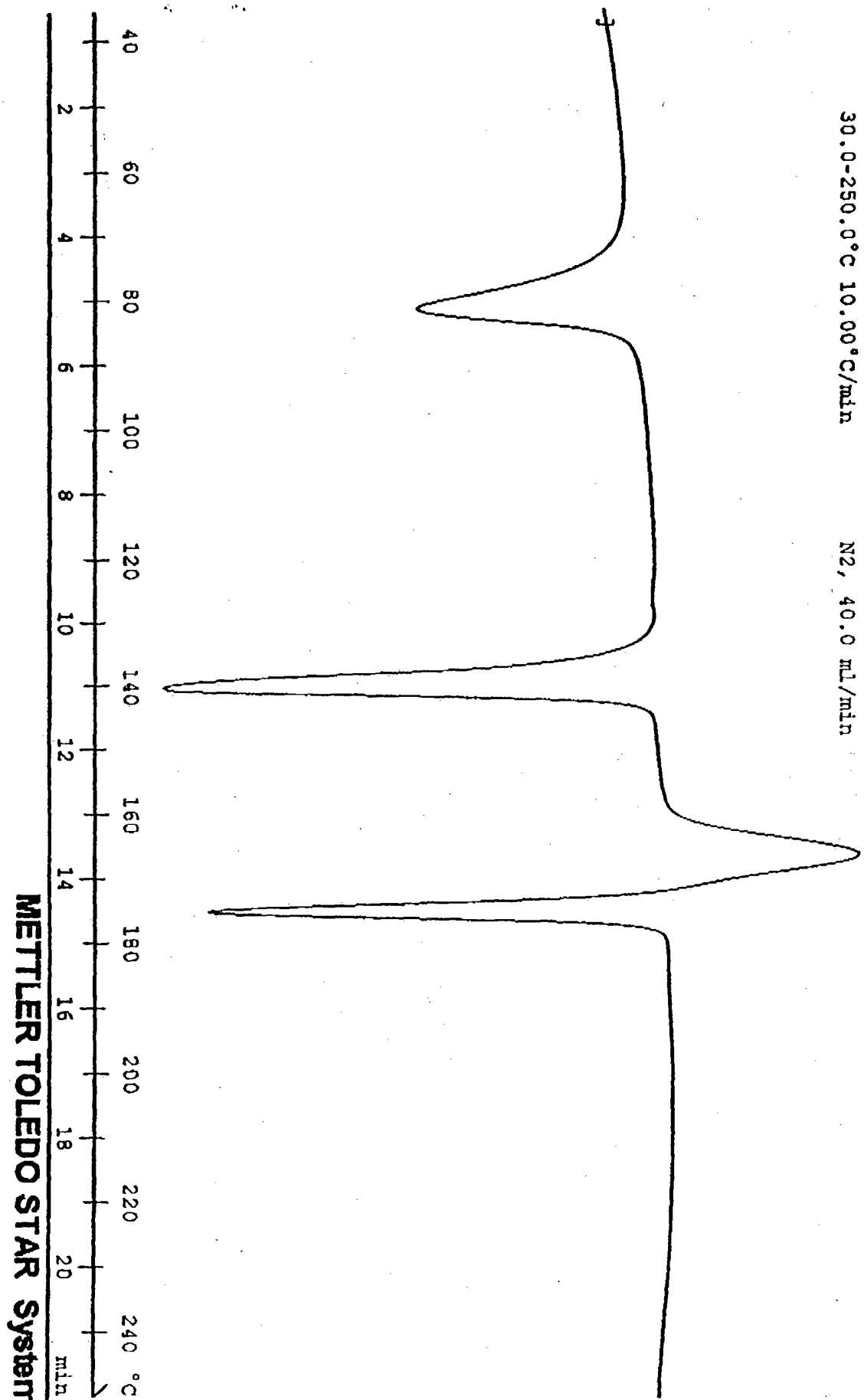


FIGURE 52-53
Form Y (chloroform solvate)

Method: 30-250°C, 10°C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min

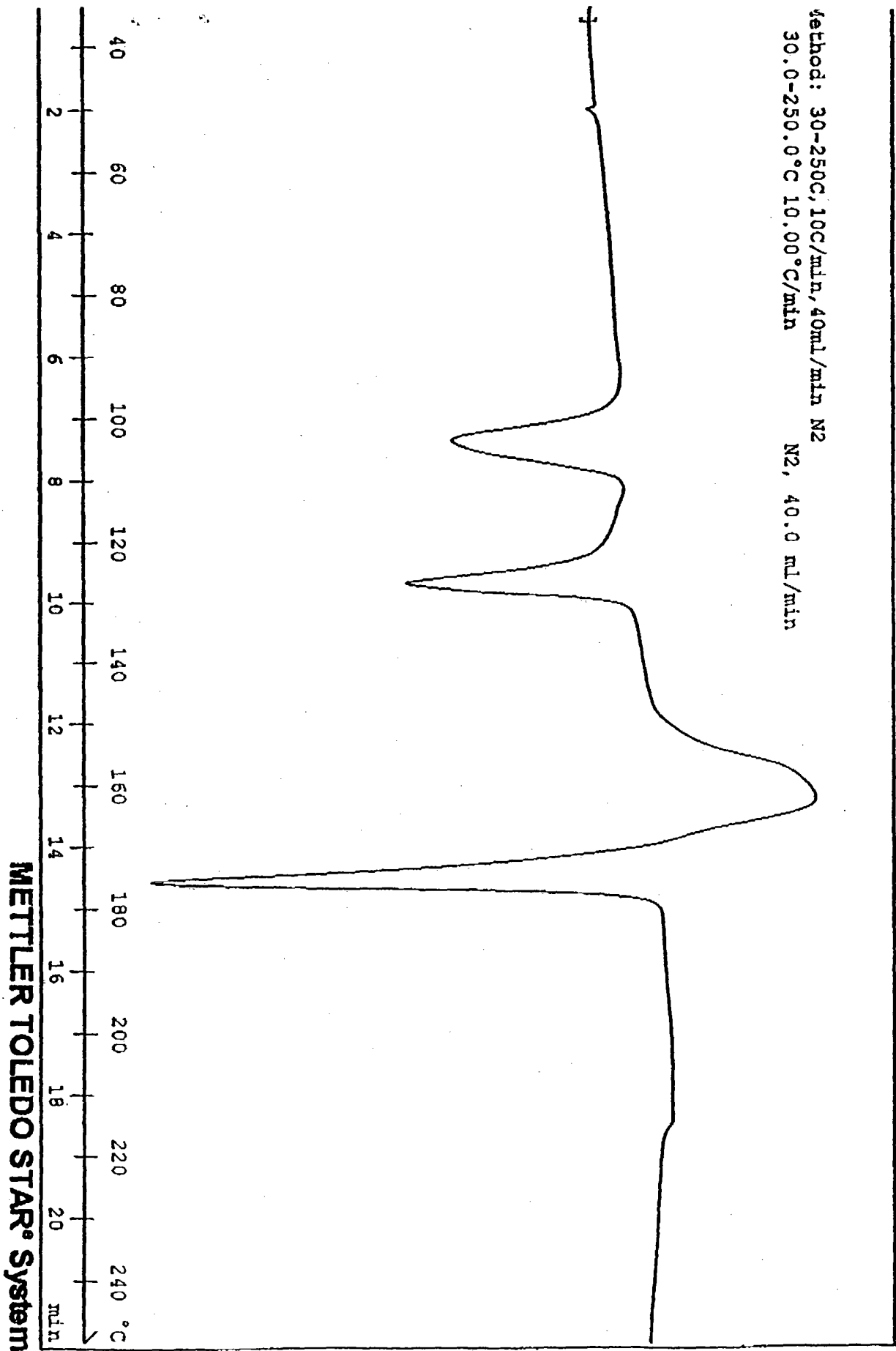
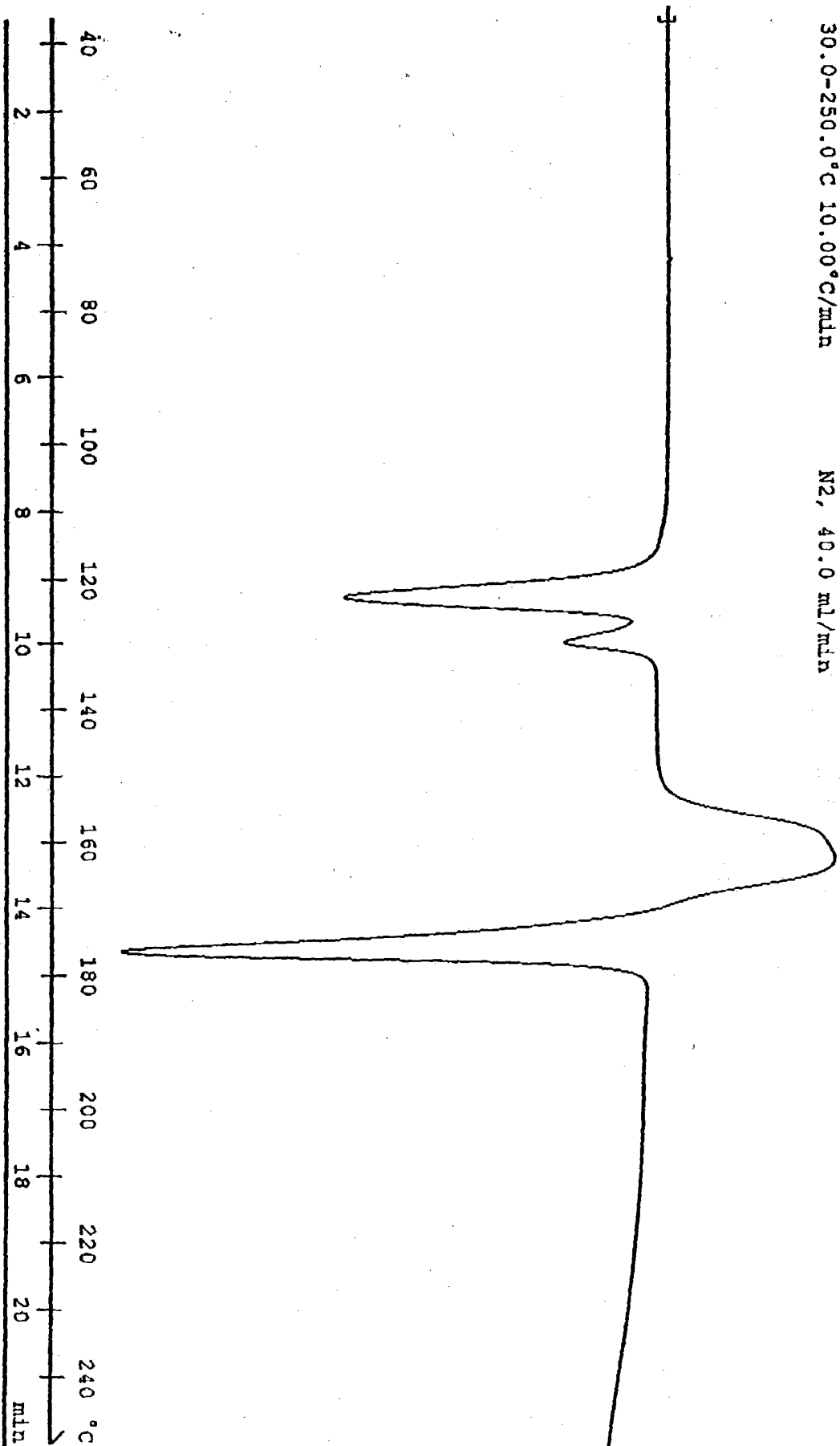


Figure 54
γ (dichloromethane solvent)

Method: 30-250°C, 100 ml/min, 40 ml/min N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min



METTLER TOLEDO STAR® System

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Figure ~~27~~ - Nataglinide Form Z

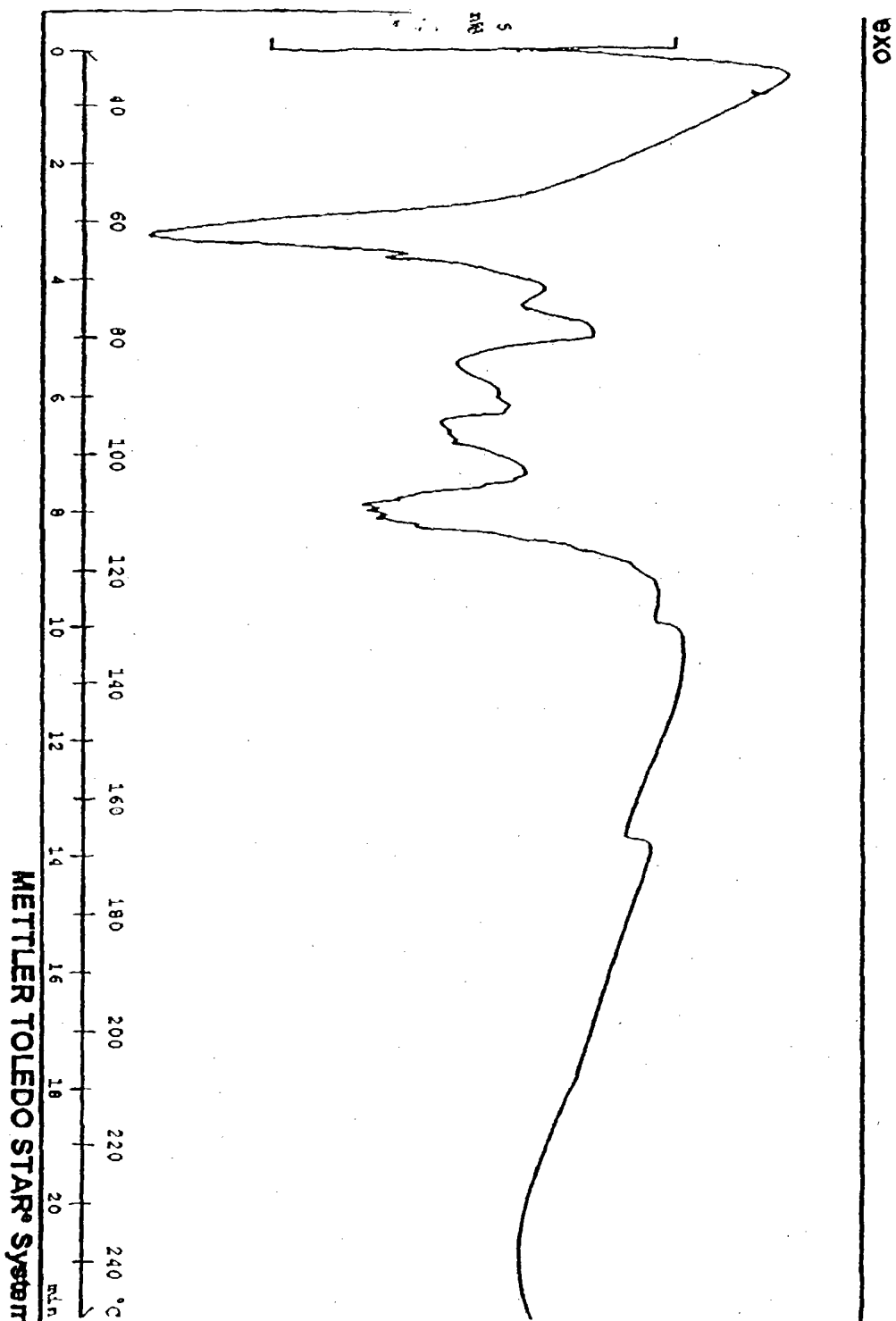
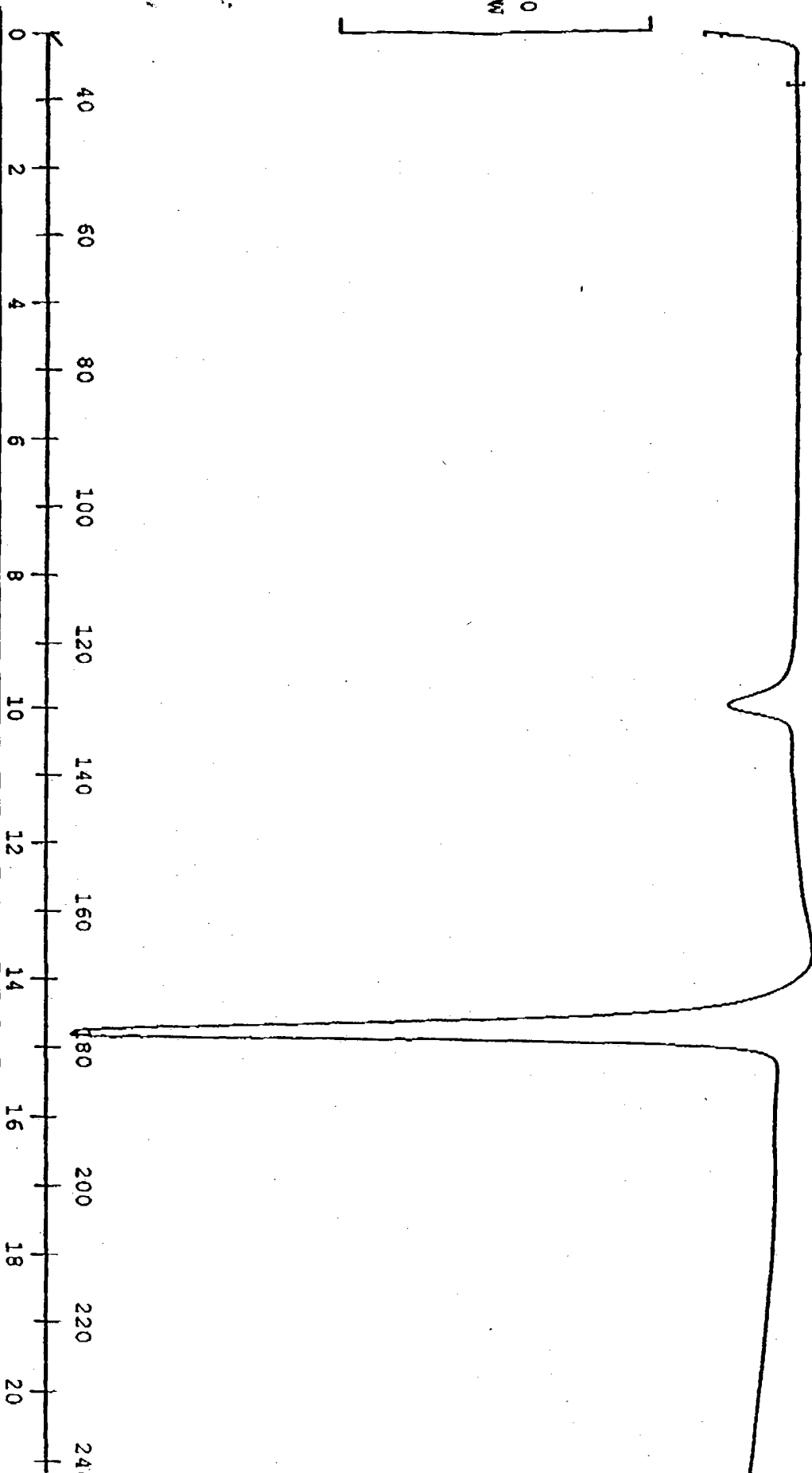


FIGURE 56
Form 2

1X0

Method: 30-250C, 10C/min, 40ml/min N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min

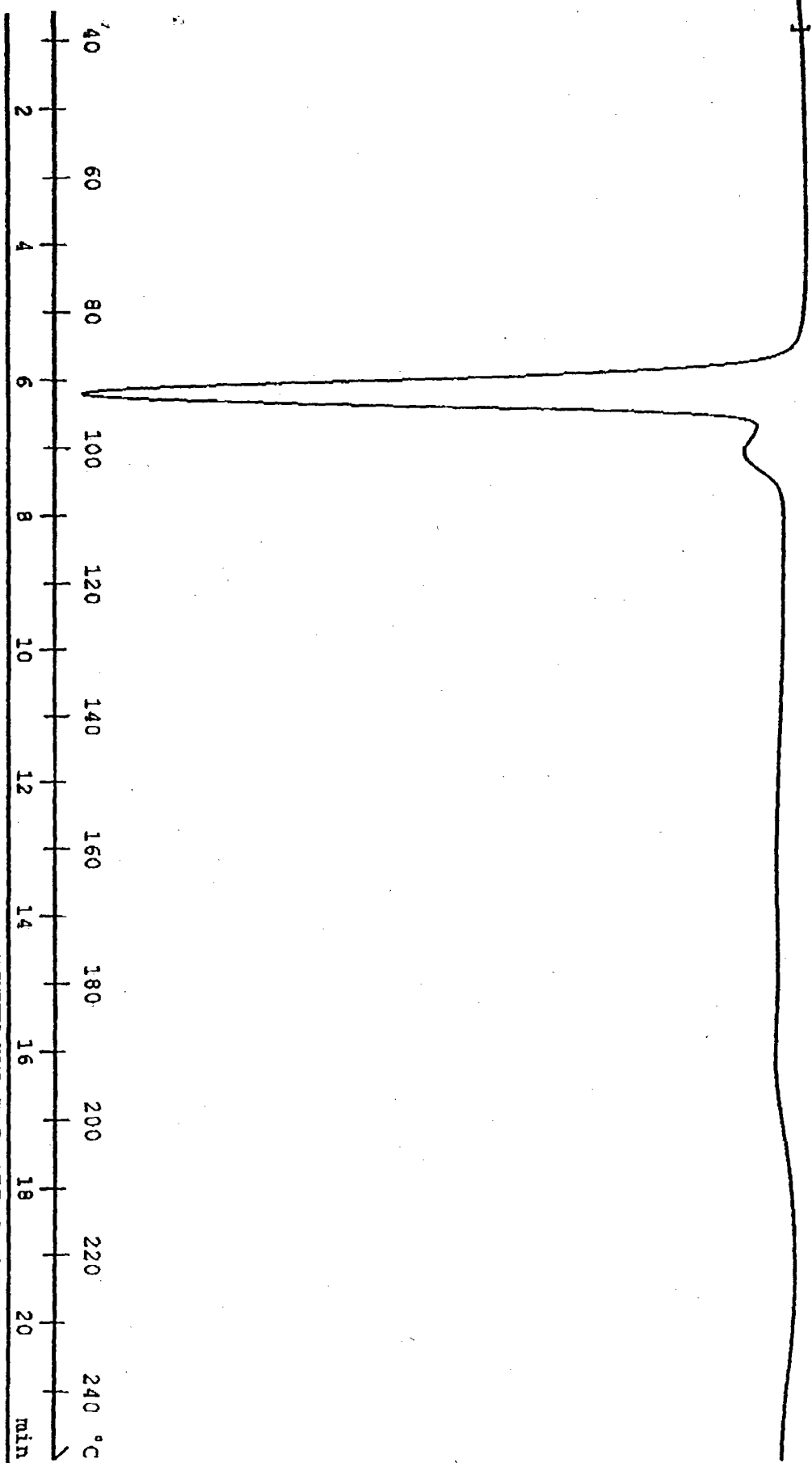
10
mm W



METTLER TOLEDO STAR[®] Sy

FIGURE 57
Form Beta

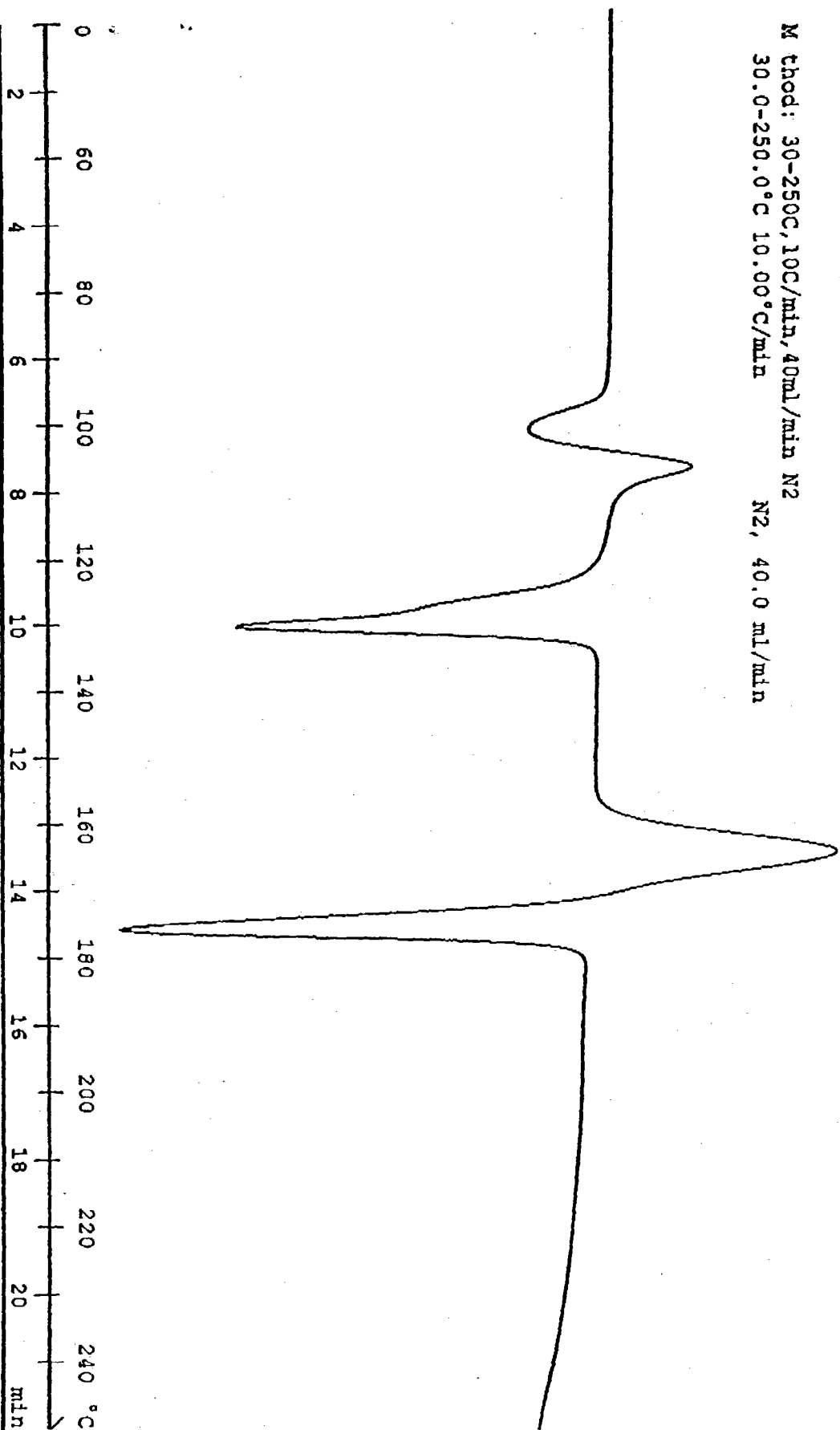
Method: 30-250C, 10C/min, 40ml/min N2
30.0-250.0°C 10.00°C/min N2, 40.0 ml/min



METTLER TOLEDO STAR® System

FIGURE 55-58
Form Delta

Method: 30-250°C, 10°C/min, 40ml/min N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min



- Delta

METTLER TOLEDO STAR System

Form Epsilon ⁵⁹ FIGURE 56

Method: 30-250°C, 10°C/min, 40ml/min N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min

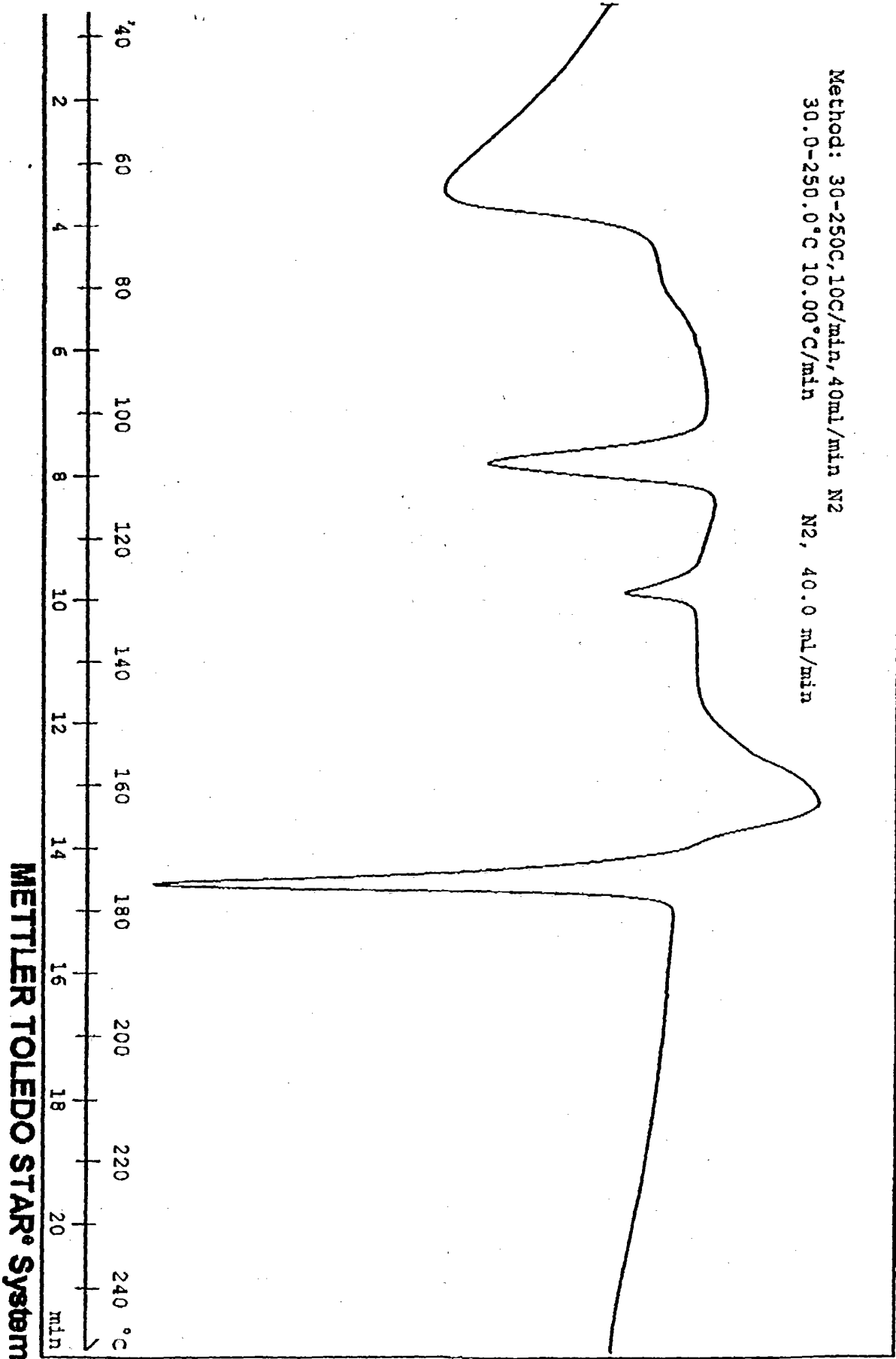
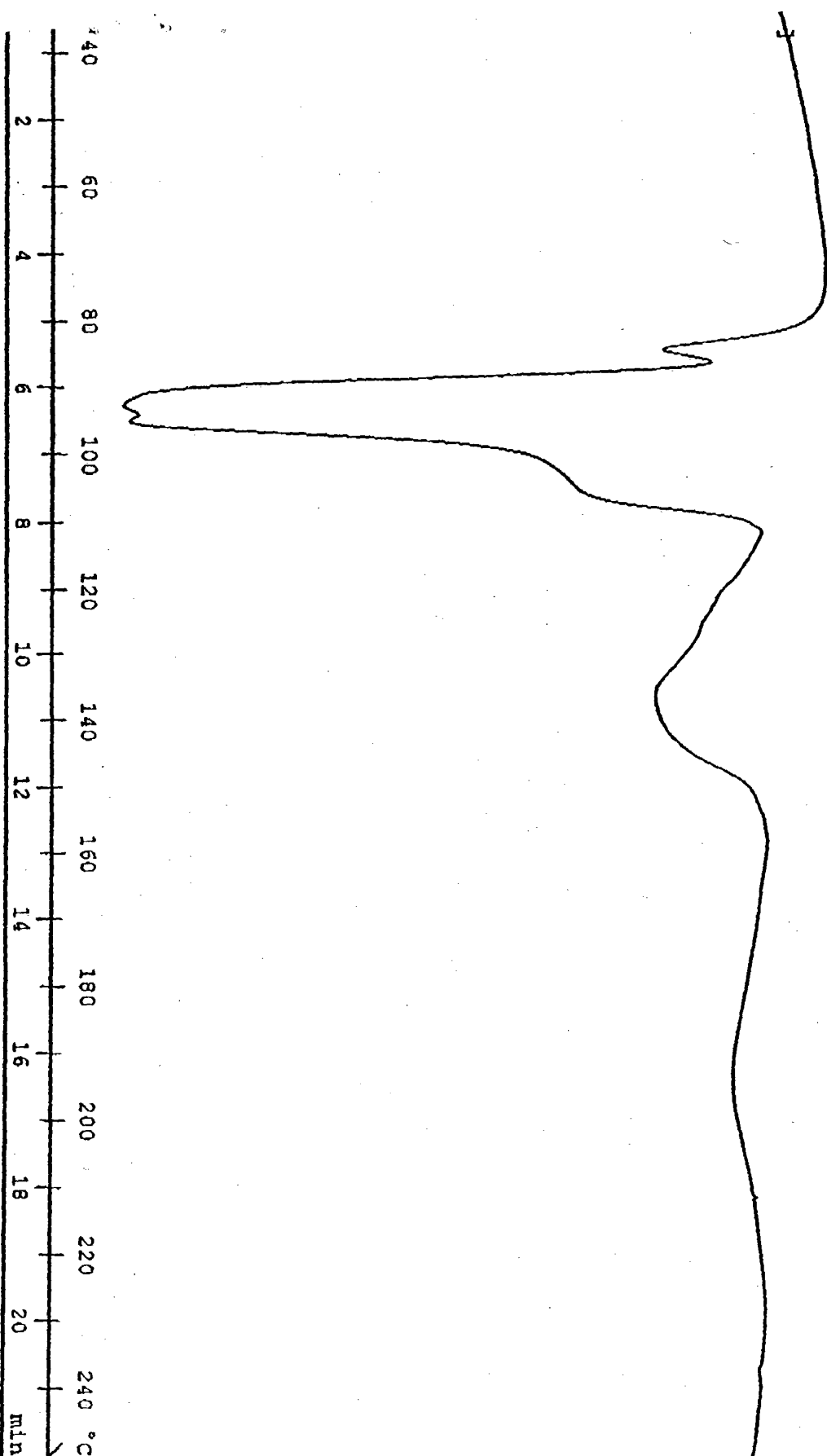


FIGURE 57 ⁶⁰
Form ~~P~~ Gamma

Method: 30-250°C, 10°C/min, 40ml/min N₂
30.0-250.0°C 10.00°C/min N₂, 40.0 ml/min

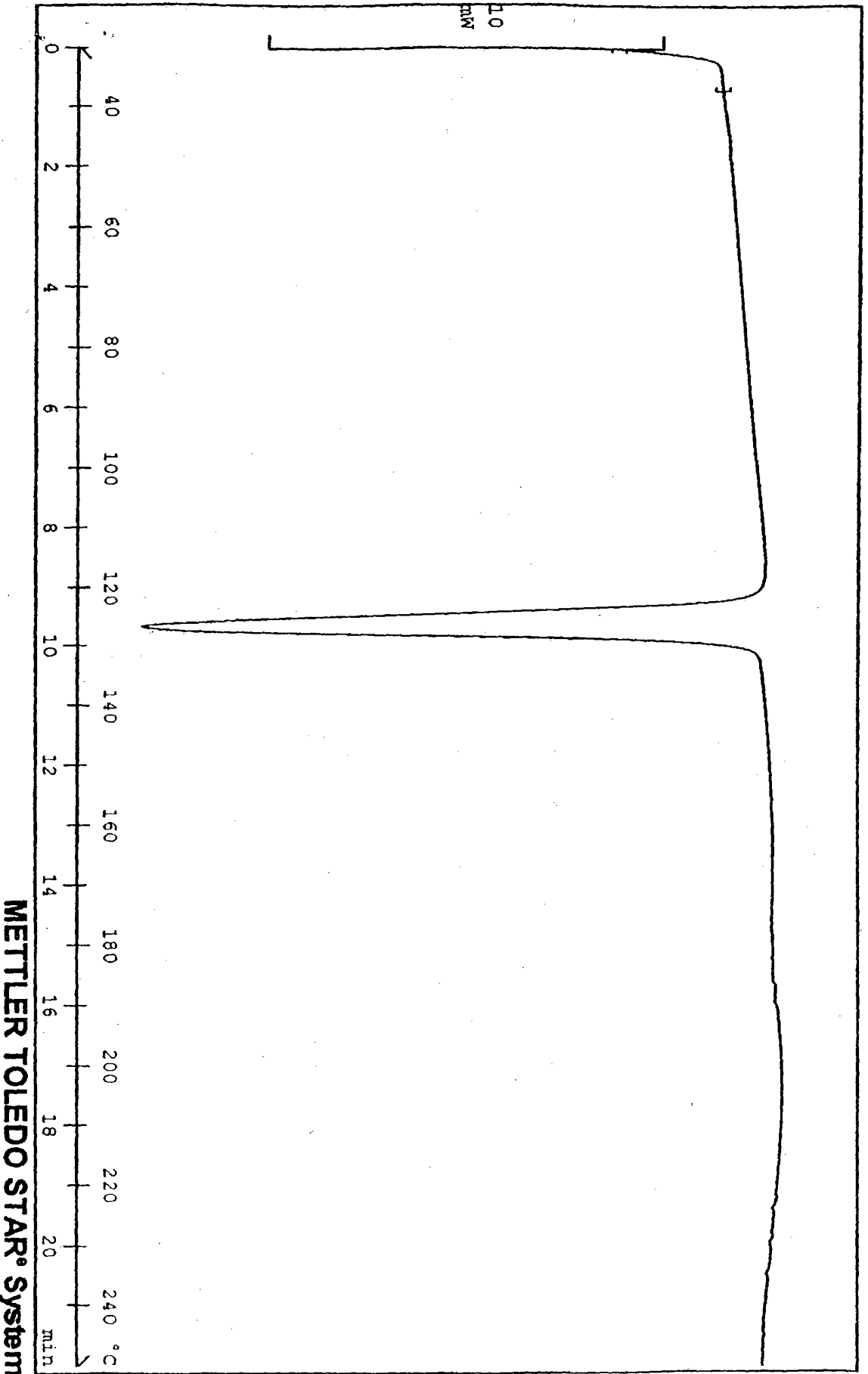


METTLER TOLEDO STAR® System

Exo

FIGURE 5e 61

Form Sigma



Form 2 (5)

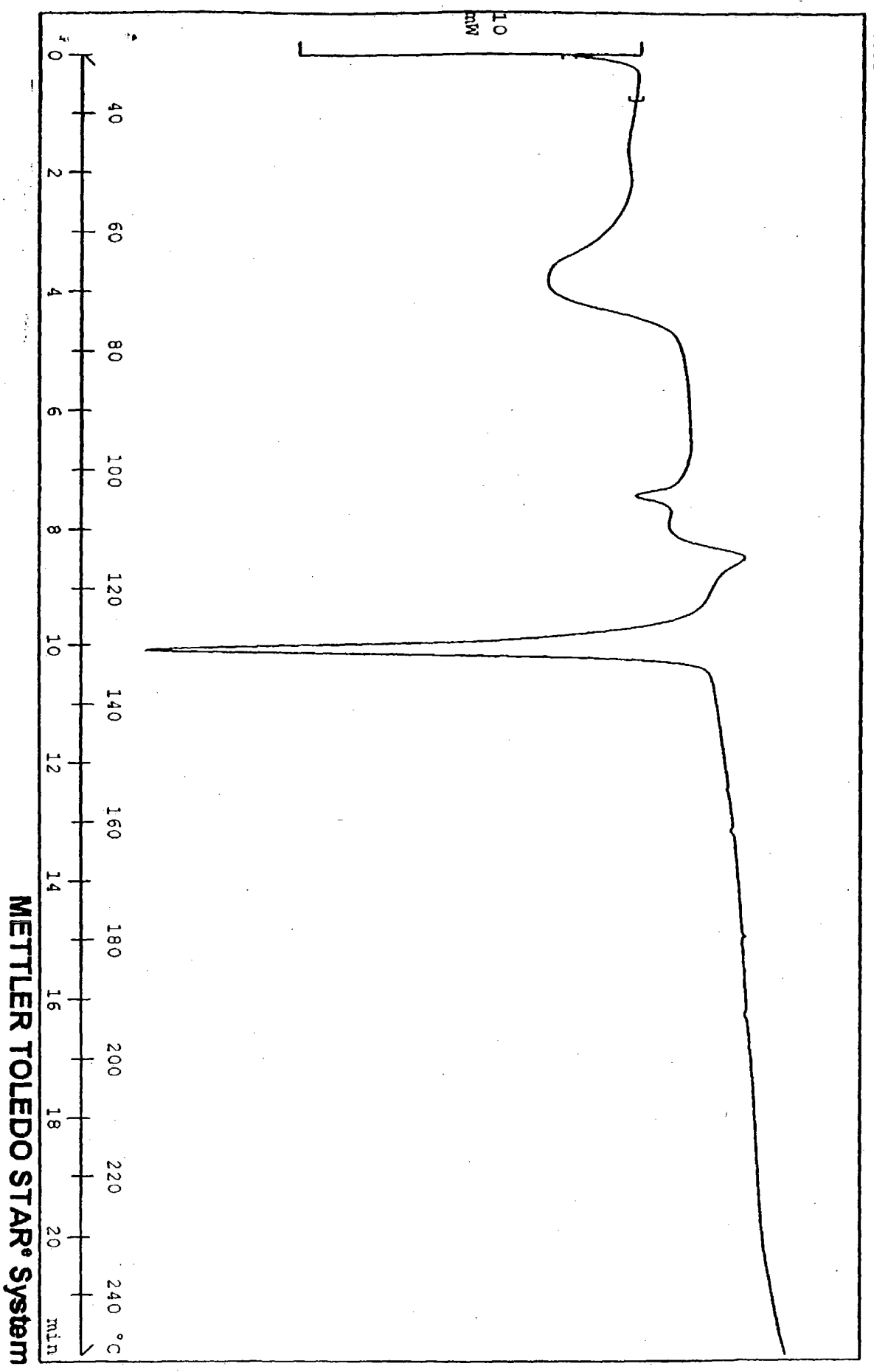
METTLER TOLEDO STAR® System

FIGURE 59

62

Form Theta

EXO



Form 8

METTLER TOLEDO STAR® System

Figure 63

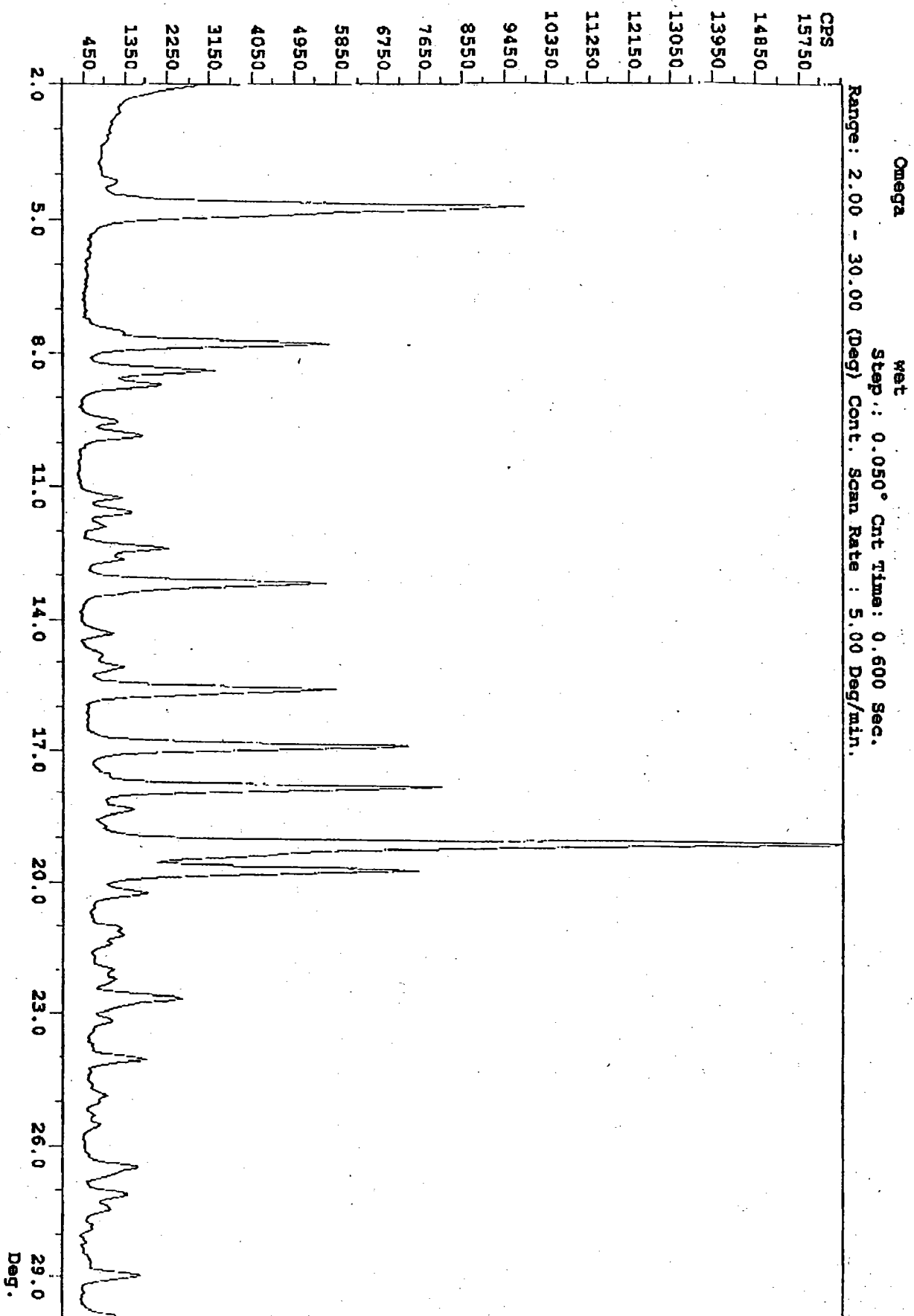


Figure 64

Comparison between the impurity profile of Nateglinide crystallized in IPA-H₂O and Nateglinide crystallized in Methanol-H₂O

Sample No	Solvent	Impurity profile by RRT [% w/w]						
		D-PA (0.23)	(0.25)	(0.46)	(0.80)	Ipcha (0.89)	Dimer (1.38)	Methyl Ester (1.51)
RL-2155/1	Methanol-H ₂ O	<0.01		0.02	<0.01	0.03	0.02	2.91
RL-2163/4	IPA-H ₂ O	<0.01	0.04		0.02	0.02	0.01	
								(1.76)
								Isopropyl Ester (2.3)
								0.04
								0.03
								0.02

Note: D-PA means D-Phenyl Alanine

Ipcha means Iso propyl cyclohexyl carboxylic acid

Both are the starting materials of the product

(-)-N-[(trans-4-isopropyl cyclohexane)carbonyl]-D-phenylalanine